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	I



RESPLITTING SPLIT-THICKNESS GRAFTS WITH THE DERMATOME

A METHOD FOR INCREASING THE YIELD OF LIMITED DONOR SITES

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THE MANAGEMENT of a large skin defect is often a difficult problem because of a limited amount of available donor skin. Methods heretofore used to cover large skin defects, namely, pinch grafts and postage stamp grafts, are not entirely satisfactory because of relatively poor cosmetic results and because of the additional time required for epithelization between the grafted areas. Split-thickness grafts produce a good cosmetic effect but the area that can be covered is limited by the available donor skin area.

It is important that large skin defects be covered as rapidly and as completely as possible. It is known that patients with extensive burns lose large amounts of nitrogen. In Hirshfeld's¹ studies upon burned patients he found that even though the patients were encouraged to eat a high protein, high carbohydrate diet, they only ingested about 60 per cent of their protein requirements. Taylor and his associates,² have demonstrated the large amounts of protein required to keep severely burned patients in nitrogen balance. The nitrogen loss is so great that malnutrition is now regarded as one of the causes of death in severely burned patients. This nitrogen loss, or protein destruction, apparently disappears as soon as the burned areas are epithelized. Early complete grafting of large skin defects will undoubtedly reduce morbidity and mortality.

In a limited number of cases the "split-split" graft, which would enable one to cover a large skin defect with a relatively small amount of donor skin and which gives a satisfactory cosmetic result has been quite successful.

The principle of the method is simply the splitting of a Padgett³ skin graft into layers. The donor skin is cut as thick as possible without interfering with the regeneration of the epithelium of the donor area. In adults this depth ranges from 0.020 to 0.028 of an inch. In the case of children, and when the abdomen or medial surface of the thigh is used in women, the depth of the graft is limited to between 0.012 and 0.018 of an inch.³ When the graft has been cut and the skin is still adherent to the dermatome drum,

the knife blade is adjusted to one-half the original distance from the drum. Rolling or separation of the leading edge of the skin from the dermatome is prevented by passing over the first quarter of an inch of skin before adjusting the knife blade to the proper distance for resplitting the skin. By repeating the cutting process the graft may be split into two layers. One must be sure that the knife edge is flat and that it is exactly parallel to the surface of the drum, otherwise the knife will tend to pull the skin away from the surface of the drum. At times it is possible to cut a Padgett graft into three layers



FIG 1—Skin 0.016 inch thick still adherent to the Padgett dermatome is being split into two layers each 0.008 inch thick.

Thus, the skin from a given donor area can be used to cover an area 200 to 300 per cent as large. The individual "split-split" grafts may vary in thickness from 0.006 to 0.012 inches.

FIG 2—A. Grafts applied to the leg of burned child. The graft in the region of the thigh is the outer thickness of a 'split-split' graft 0.008 inch thick. On the popliteal region is an ordinary Padgett graft 0.016 inch thick. The region of the calf is covered with the inner thickness of a 'split-split' thickness graft 0.008 inch thick.

B. All three areas of grafts have taken 100 per cent on the tenth postoperative day. The raw area in the region of the calf is the result of too early removal of the paraffin gauze. When the paraffin gauze was removed a thin layer of epithelium was removed with the gauze. The deeper epithelial elements are clearly seen.

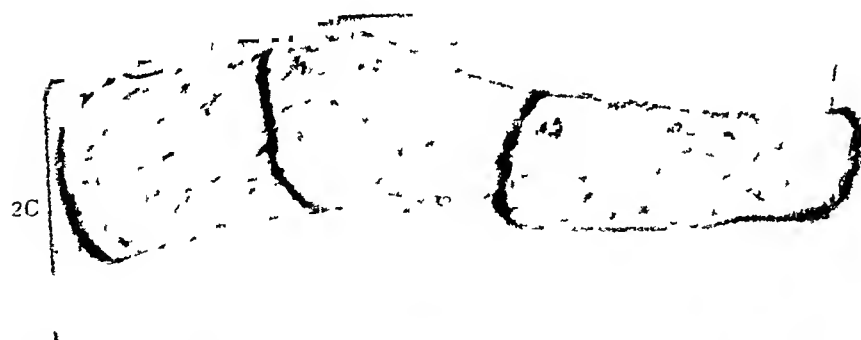
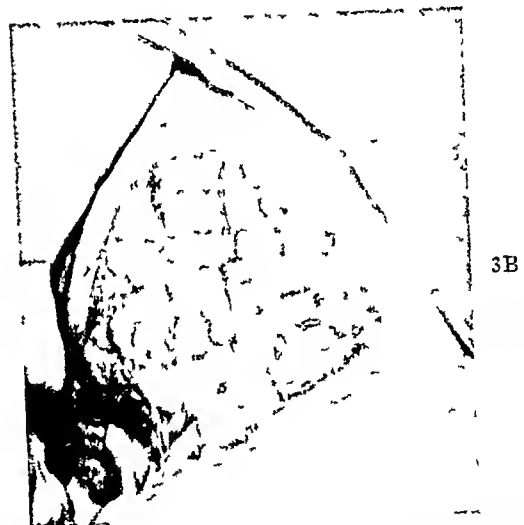
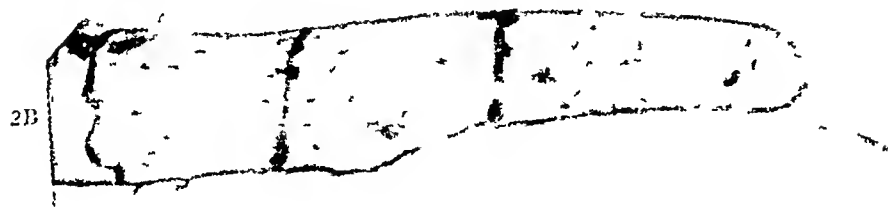
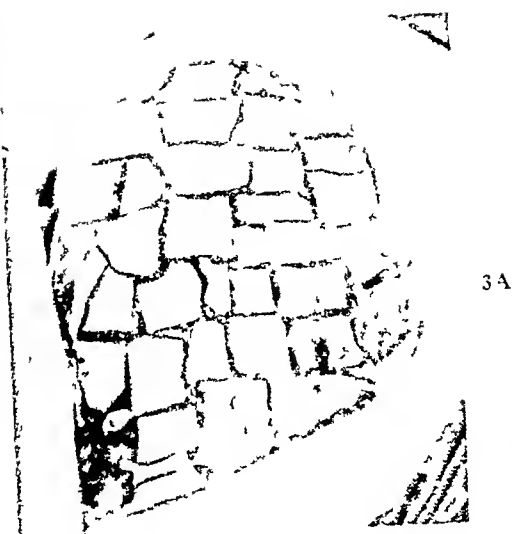
C. Appearance of grafts four weeks later. All areas have been completely epithelized. Raw areas seen in the region of the ordinary Padgett graft as well as in the regions of the 'split-split' grafts, are the result of secondary infection. These raw areas were at one time epithelized as can be seen in B.

FIG 3—A. "Split-split" grafts may also be used as postage stamp grafts. The postage stamp grafts from the inner layer of the 'split-split' grafts have been applied over the right half of the ulcer as it appears in the photograph and outer layer of the 'split-split' grafts over the left half of the ulcer of the buttock.

B. Appearance of the same grafts five days later.

C. Complete healing three weeks later.

FIG 4—Typical 'split-split' donor area three weeks after cutting of the graft.



The take of the inner layer of a "split-split"-thickness graft produces a result which is quite similar to the healing Padgett donor area. During the first ten or twelve days both of these areas are covered with a thin sheet of epithelial cells. This delicate epithelial layer is easily injured by frequent dressings. We have learned to dress the donor area with paraffin gauze and leave the innermost layers of the dressings in place, literally, until they fall off, which is usually at the end of two weeks. The "split-split" grafts like the donor areas are covered with two layers of paraffin gauze. A pressure dressing of ordinary gauze is then applied over the paraffin gauze. The grafted area is not touched until the tenth postoperative day. At this time the outer dressings are removed. If the grafts are not infected the paraffin gauze is not removed for fear of injuring the delicate new epithelial layer. The paraffin gauze may be removed without danger of injuring the new epithelium after the fifteenth to sixteenth postoperative day.

"Split-split" grafts have been employed on six patients. In one of these patients, the result was classed as a failure, although parts of the grafts did take. In this same patient a subsequent simple Padgett graft was equally unsuccessful. In the remaining five cases 90 to 100 per cent of the grafts remained viable. The outer layers and the inner skin layers took equally well. The period required for the inner layer to become completely healed is slightly more prolonged than that required for the outer layer of the skin. This is due, probably, to the fact that the outer layer of skin is completely keratinized at the time of the application of the graft, whereas the inner layer is not.

Some operators have failed to obtain satisfactory results with the Padgett dermatome. Since we have adopted a rigid technic for preparing the skin and the dermatome drum, we have not failed to obtain complete grafts. Two factors seem important. The first is a clean, fat- and moisture-free skin surface. The second is the time factor which is necessary to allow the dermatome (rubber) cement to set before the actual cutting is attempted.

In preparation of the donor skin the area must be closely shaved (preferably with a straight razor) and then be washed with soap and thoroughly rinsed with water either in the patient's room or in the operating room. In the operating room the area is treated with alcohol followed by several liberal applications of ether. Special skin preparations and preparations containing dyes or bichloride of mercury have been carefully avoided for fear that they might leave a thin film or precipitate on the skin which would interfere with the efficiency of the dermatome cement. Each application of alcohol and ether is combined with vigorous scrubbing of the skin with a gauze sponge on a sponge stick. The ether assures one of the adequate removal of all fatty material. It may also act locally to cool the skin so as to inhibit excretion of the sweat glands temporarily. Perspiration may lift

the cement away from the skin surface sufficiently to prevent the adherence of the skin to the dermatome drum

The cement must be allowed to set or partially dry before the actual cutting is attempted "Haste makes waste" were never truer words than in the cutting of Padgett grafts Five to ten minutes are allowed for the setting or partial drying of the cement The dermatome drum may even be painted before the patient is anesthetized

Another possible cause of failure of adherence of the cement is the application of the cement to a recently autoclaved dermatome which is still warm The heat of the drum will cause the rubber solvent to boil and form bubbles in the cement If bubbles form in warm weather the drum should be cleansed with ether and then two very thin layers of cement should be applied Care should be taken that one layer of cement is quite dry before another is applied The cement-covered skin and drum should not be touched for fear of removing some of the cement

When the layers of cement have dried sufficiently the leading edge of the drum is firmly applied to skin for at least one minute by the clock The drum must not be twisted or rocked upon the skin lest some of the cement become detached from the skin or drum The cutting should be done slowly, in order to provide ample time for the skin to become firmly adherent to the rolling drum surface Short even strokes of the knife blade are used to cut the skin Wide excursions of the cutting knife tend to separate the skin from the drum If the foregoing rules are observed a complete drum of skin can be easily removed

SUMMARY

- 1 A method of splitting ordinary Padgett split-thickness skin grafts is described
- 2 Certain details of the technic for the use of the dermatome are presented which enable us, consistently, to obtain a full drum of skin
- 3 By using "split-split"-thickness grafts areas which are 200 per cent to 300 per cent larger than the donor area, can be epithelized
- 4 The inner layer of a "split-split"-thickness graft becomes completely epithelized in about the same period of time required for epithelization of the Padgett donor area
- 5 In five of six patients 90 to 100 per cent of the "split-split"-thickness grafts remained viable One case in which an ordinary Padgett split-thickness graft was unsuccessful, "split-split" thickness grafts were also unsuccessful

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COMPARATIVE STUDIES OF CANCEROUS VERSUS NONCANCEROUS BREASTS

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I BASIC MORPHOLOGIC CHARACTERISTICS

THE PRESENT STUDY represents an effort to determine whether fundamental structural differences exist in the breast tissue of women who do have mammary cancer and those who do not have this disease. In other words, the main objective has been to ascertain if there is any characteristic "soil" in which mammary carcinoma is apt to develop. Another interest has been to search for abnormalities in these breasts that could be referred to certain hormonal influences, and finally an attempt has been made to evaluate the relationship between so-called chronic cystic mastitis and mammary cancer. The investigation was not begun with any preconceived point of view concerning these problems, and it has been constantly borne in mind that little positive information might be secured. A study of this sort necessarily enters into debatable matters about which a vast literature has accumulated. Due to the large volume of such literature, reference can be made only to specific papers which seem most pertinent to the findings under discussion.

The material for comparative gross and microscopic analysis was secured during 1940 from operations performed on the Breast Service at the Memorial Hospital. It consisted of 300 cancer-containing breasts from radical mastectomies and 200 specimens of noncancerous breast tissue from partial mastectomies or very occasional simple mastectomies. The material was sectioned specifically for this planned study, and in every case both normal and abnormal appearing tissues were embedded. No selection of cases was made with the following exceptions. No irradiated breast was included. A few cases were excluded in which there was total or near total replacement of the breast tissue by carcinoma. In the cases of local excision, it was required that the mass of breast tissue be large enough to furnish satisfactory representative sections. Thus, it was necessary to exclude a small number of assorted noncancerous lesions excised with a margin too small for our purposes. Finally, no case was included in which the operation was undertaken for pyogenic or specific infection of the breast.

We recognize the disadvantage of comparing the findings in complete mastectomies with findings in partial mastectomies. This disproportion in tissue mass, however, is largely compensated for, since in doing a local excision, the surgeon may be expected to select the most obviously abnormal portion of the breast and is careful to remove a margin of less involved or uninvolved tissue. So if a gross abnormality is present it appears likely that it will be removed. In order to balance microscopic findings as much as possible, compar-

able amounts of grossly unaltered tissue were embedded in both the cancer and the noncancer cases. The total mass of tissue embedded in the two groups of cases has been equal in amount exclusive of the cancer itself.

In this survey the following plan of analysis was employed. Each case was tabulated for the presence or absence of specific lesions, so that composite percentage figures for each of the two types of cases were secured. The two general groups were then subtabulated, decade by decade, to enable proper comparison, since the influence of age in the frequency of certain lesions is so great that this must be insisted upon in interpreting results. For closer analysis of certain specific lesions, it was then considered necessary to tabulate other lesions that occurred in unison with the particular one under examination. By this method it is possible to learn the sort of histologic environment in which a given lesion is apt to be found and it permits one to detect trends in occurrence that indicate fundamental interrelationships, or their lack. By no means do the figures given for the incidence of certain lesions imply that they represent absolute values. The frequency of microscopic lesions can always be elevated somewhat by embedding innumerable blocks. Terminology in breast lesions is by no means standardized. Where commonly employed terms are used, effort has been made to define our own usage of these, and where unaccustomed ones are used, special effort has been made to describe the lesions in full.

The average age of the 300 cancer cases was 49.5 years, that of the 200 noncancer cases 39 years. The distribution by decades is shown below.

TABLE I

Decade	Cancer Cases	Noncancer Cases
10-20		4
20-30	3	30
30-40	54	68
40-50	104	78
50-60	66	16*
60-70	60	3
70+	13	1
Total	300	200

* In tabular analyses that appear in succeeding sections comparative histologic findings are given for the third, fourth, and fifth decades. Since the series of 200 noncancerous breasts contained only 16 cases in the fifth decade, 24 consecutive noncancerous breasts were added to this group, so that observations are based on the more significant number of 40 cases.

Subjects to be discussed will appear in the following order:

- I Factor of atrophy
- II Cysts
- III Duct papillomatosis
- IV Blunt duct adenosis
- V Apocrine epithelium
- VI Sclerosing adenosis
- VII Periductal mastitis
- VIII The mammary lobules
- IX Relation of so called chronic cystic mastitis to mammary cancer
- X Histologic findings in breasts after administration of estrogenic substance

I — FACTOR OF ATROPHY

Inasmuch, as mammary cancer occurs most frequently in breasts that are beginning to undergo atrophy, or are already in varying degrees of this state, can any differences in this process be found in cancerous as opposed to noncancerous breasts? The principal feature in atrophy of the mammary gland is reduction of its parenchyma to an extent that is much more complete than in most organs. Atrophy begins at the lobular terminations of the duct system and proceeds toward the nipple so that the end-result is near, or total, loss of lobules and more or less diminution of the terminal and small ducts. Extreme variations in the degree of atrophy can be seen in individuals of the same age-group, and occasionally breasts are seen that maintain the integrity of their lobules for surprisingly long periods beyond the menopause. As an illustration, we have recently studied sections from a surgical excision done three years after the menopause. In this case the lobules were not only very numerous but they possessed abundant acini, and, here, mitoses were found in surprisingly large numbers. In the absence of various quantitative and qualitative metabolic determinations, no explanation attempted could be supported. The patient had a strong family history of mammary cancer. In atrophy of the breast other changes, such as loss of periductal myoid, duct dilatation, fatty replacement of fibrous stroma, and subsidence of certain proliferative and cystic lesions, accompany the decreasing number of mammary lobules.

An estimate of the number or frequency of the mammary lobules is the most convenient index for estimating atrophy. No very exact method of estimating the number of lobules seems required, nor is it reasonably possible, and we have merely listed cases as having "numerous," "average" or "few" lobules. Table II shows the frequency of lobules in the cancer and noncancer cases as separate whole groups and also shows a comparison by decades.

TABLE II

	Number of Lobules		
	Numerous	Average	Few
200 noncancer cases	13%	61%	25%
300 cancer cases	8%	36%	56%
Noncancer cases age 30-40	10%	60%	30%
Cancer cases age 30-40	10%	51%	39%
Noncancer cases age 40-50	12%	55%	33%
Cancer cases age 40-50	10%	57%	33%
Noncancer cases age 50-60	3%	25%	72%
Cancer cases age 50-60	3%	27%	70%

The only significant discrepancy shown is in the lobule frequency of the two types of cases when compared as whole groups. This is at once referable to the greater average age of the cancer-containing breasts, since, in equivalent decades, there is close uniformity. It appears justifiable to state the obvious conclusion that mammary lobules are not more or less numerous in cancerous than noncancerous breasts in the same age-group.

It may be inquired if any of the common proliferative lesions of the breast

tend to persist in cancerous breasts and disappear from noncancerous breasts, presumably supplying a possible source for the development of cancer. This is given a negative answer in other sections of this paper where these lesions are shown to regress sharply in the 50- to 60-year decade.

The question of the relation of mammary atrophy to mammary carcinoma is of very considerable speculative interest. It is of interest from at least two viewpoints. Certain it is that atrophy is a precursor of cancerization in certain tissues, although causal relationship of such atrophy to cancer is not clear. Our observations as regards mammary atrophy fail to indicate that such atrophy is significantly more frequent in the cancerous breast when compared to the noncancerous breast of similar age. The second point of interest concerns the question of hormone etiology of mammary cancer. Where those hormones which presumably are concerned with mammary lobule growth or persistence concerned in a major way with mammary cancer development, one might at least expect some difference in lobular status in the cancerous versus the noncancerous breast, that is, one might anticipate the finding of greater lobule abnormality outside the actual cancerous area in the cancerous breast than in the "normal" for the age-group. This matter will be discussed in some detail in a later section pertaining specifically to lobule structural patterns.

II — CYSTS

Included in these tabulations are only those cysts visible to the naked eye, and, hence, those cysts measuring from about one millimeter upwards in diameter are represented. It is our belief that if one reports on microscopic cysts, serial sections are required to prove complete isolation and loss of communication with adjacent ducts or lobules. If microscopic lesions that appear cystic are included, it is inevitable to confuse, in some measure, blunt end ducts, dilated ducts or distended lobule components. No lesion was included as a cyst unless it was an isolated structure distended with fluid and totally separate from duct and lobule system. The figures will not separate cases with solitary cysts from those with multiple ones, since in both types of material the solitary cysts, whether large or small, were so few as to be insignificant.

In the 200 noncancerous breasts, cysts as qualified in the preceding statements were found in 106, or 53 per cent. Of the 300 cancer breasts, 82, or 27 per cent, contained cysts. The average age of the benign cases with cysts was 41.1 years and in the cancer cases with cyst, the average age was 48.4 years. When the occurrence of cysts is studied by decades, the following is seen (Table III).

TABLE III

Decade	Comparative Frequency of Cysts in	
	Noncancerous Cases	Cancer Cases
30-40	52%	34%
40-50	65%	18%
50-60	30%	25%

Accordingly, it is obvious enough that cysts are distinctly more characteristic of noncancerous than cancerous breasts. Indeed, in the decade 40-50,

which is the most common ten-year period for the appearance of mammary cancer, they are less than one-third as frequent in cancer-bearing breasts as in breasts free from cancer. Cysts, like many other lesions of the breast, may appear at a relatively early age, but are often transient structures and they become decreasingly numerous as old age is reached. Observations extended beyond the age of 60 (in material additional to that studied here) show that between 60-70 years of age, the incidence of cysts in both cancerous and noncancerous breasts falls sharply. Statistically, cysts seem to play a negative rôle in mammary cancer. The lower incidence of cysts in cancer-bearing breasts cannot be explained by the supposition that the cysts are replaced by the cancers, for morphologic evidence is directly opposed. In tracing the genesis of mammary cancer, one finds true intracystic carcinoma to be one of the rarest morphologic types. Terminology in breast pathology is so loose that the term "intracystic" is often employed when the proper designation is "intraductal." This common practice has led to much confusion as to the frequency of intracystic cancers as well as intracystic papillomas. If one studies the walls of cysts he finds with extreme rarity any evidence of atypical or other epithelial proliferation. It is actually much more common to find no epithelial lining at all. In the 300 cases of mammary cancer under consideration here, only two could be shown convincingly to have arisen in a cyst.

The question may be raised as to what other lesions are apt to be found in breasts that contain cysts and if the same lesions appear regardless of whether the breast is or is not cancer-containing. For making these determinations, all of the cyst-bearing breasts were tabulated for the presence or absence of 14 definite histologic characters. In Table IV are also shown figures for the frequency of these lesions as they occurred in the entire group of 200 cases without cancer and the 300 cases with cancer.

TABLE IV

	106 Noncancer with Cysts	200 Consecu- tive Cancers	82 Cancers with Cysts	300 Consecu- tive Cancers
1 Hyperplasia of duct epithelium	52%	39%	80%	57%
2 Duct papillomatosis	42%	29%	50%	36%
3 Intracystic papilloma	2%	2%	1%	1%
4 Blunt duct adenosis	40%	26%	40%	26%
5 Apocrine epithelium	67%	42%	57%	39%
6 Sclerosing adenosis				
A Diffuse	1%	1.5%	2%	0.3%
B Focal	18%	11%	13%	7%
7 Fibro adenoma	9%	19%	10%	7%
8 Tendency to fibro adenoma	5%	3%	8%	6%
9 Stasis and distention of ducts	41%	36%	62%	42%
10 Duct metaplasia	42%	34%	62%	45%
11 Periductal mastitis	23%	22%	20%	14%
12 Fat necrosis	1%	2%	2%	1.3%
13 Lobule frequency				
Numerous	14%	13%	10%	10%
Average	62%	61%	41%	35%
Infrequent	24%	26%	49%	55%
14 Periductal myoid atrophy	31%	27%	56%	42%

From Table IV a general summary may be drawn that no obvious qualitative divergence is detectable when comparing the noncancerous elements of cancer-containing breasts with breast tissue removed surgically from noncancerous breasts when the common denominator of each group is the presence of one or more cysts. True enough, there are certain quantitative differences of lesser degree which are substantially diluted when the factor of age is considered. Cysts may be regarded as relatively passive structures representing essentially the end-phase of a pathologic process. Characteristically, they are accompanied by a group of what may be termed proliferative processes somewhat more numerous than the proliferative processes seen in a general average of breasts when these proliferative processes are enumerated with disregard of the presence of cysts.

It is of interest to compare the lesions in noncystic breasts with the findings just recorded for cystic breasts of both benign and cancerous breasts.

TABLE V

	Frequency of Various Lesions in			
	106 Noncancer, with Cysts	94 Noncancer, without Cysts	82 Cancers, with Cysts	218 Cancers without Cysts
1 Hyperplasia of duct epithelium	52%	23%	80%	48%
2 Duct papillomatosis	42%	14%	50%	31%
3 Intracystic papilloma	2%	2%	1%	1.5%
4 Blunt duct adenosis	40%	9%	40%	20%
5 Apocrine epithelium	67%	14%	57%	32%
6 Sclerosing adenosis				
A Diffuse	1%	1%	2%	0%
B Focal	18%	6%	13%	4%
7 Fibro-adenoma	9%	30%	10%	6%
8 Tendency to fibro-adenoma	5%	5%	8%	5%
9 Stasis and distention of ducts	41%	28%	62%	34%
10 Duct metaplasia	42%	25%	62%	39%
11 Periductal mastitis	23%	19%	20%	12%
12 Fat necrosis	1%	3%	2%	1%
13 Lobule frequency				
Numerous	14%	12%	10%	11%
Average	62%	52%	41%	35%
Frequent	24%	36%	49%	64%
14 Periductal myoid atrophy	31%	22%	55%	36%

Table V emphasizes in greater contrast than the preceding one the tendency of certain lesions to occur in cyst-containing breasts irrespective of the presence of cancer. These lesions include hyperplasia of duct epithelium, duct papillomatosis, blunt duct adenosis, apocrine epithelium and sclerosing adenosis. All of these can be regarded as proliferative or hyperplastic in nature. It should be noted that fibro-adenoma fails to follow this tendency and in the benign group is actually reversed. Fibro-adenoma must be regarded as a proliferative lesion, but it seems to be of a different order from other mammary proliferations. Also to be noted is the greater frequency in cyst-containing breasts of lesions designated as "stasis and distention," "duct metaplasia," "periductal myoid atrophy" and "periductal mastitis." That these are secondary phenomena dependent upon pressure and obstructive factors will be explained in a section to follow.

III — DUCT PAPILLOMATOSIS

Under this designation are included all stalked papillary adenomas. These are usually found in the large- or medium-sized ducts and are usually macroscopic. Also, included here are cases with partial or complete epithelial plugging of the smaller stems of the duct system. These lesions are often seen with no vascular stalk, and it is admitted that they are not papillary adenomas in the strictest sense of the word. They are, however, papillary in a modified sense and of distinctly greater magnitude than lesions spoken of here as simple hyperplasia of duct epithelium. In a large part they are microscopic and almost invariably multiple. They are present in many more cases than are the macroscopic stalked papillomas, but in nearly every case where a stalked papilloma is present these lesions can be found in some other portion of the breast tissue. No universally accepted standard exists for the lower level of epithelial hyperplasia where one ceases to use the term papillomatosis, and any division must be more or less arbitrary. Undoubtedly, writers on breast pathology do not uniformly conform in terminology. It is our belief, that in the material here, a relatively strict interpretation is made, and that in many other hands the figures for the papillary lesions might be considerably higher. In any event, the same level of inclusion or exclusion is adhered to when enumerating these papillary lesions in the two types of material under examination here. The stress is always to compare the same kinds of lesions. Emphasis is again made that in this section we are considering papillary lesions that are intraductal in location, and the statement is repeated that true "intracystic papillomas" are of very uncommon occurrence. It would be necessary to have several thousand consecutive cases of cancerous and noncancerous breasts to yield a sufficiently large number of true intracystic papillomas before adequate comparisons could be made.

In the series of 200 breasts without cancer, duct papillomatosis was found in 58, or 29 per cent. In the 300 breasts containing cancer, this finding was made in 108, or 36 per cent. It should be noted that the figures quoted would be appreciably elevated if papillary hyperplasias of pink-staining apocrine epithelium were included. Foci of apocrine epithelium are sometimes found in a papilloma, to be sure, but no case was included in which the papillary element was solely apocrine. The mammary apocrine element is discussed in a separate section. Although repetitive, the statement is emphasized that the lesions, recorded here as constituting papilloma or papillomatosis are not minimal in nature, and would certainly be regarded by any reasonable observer as meriting the dignity of the term.

The occurrence of papillomas by decades is recorded in Table VI.

TABLE VI

Decade	Frequency of Duct Papillomatosis in	
	Noncancerous Cases	Cancer Cases
30-40	18%	24%
40-50	40%	40%
50-60	23%	28%

Table VI indicates no very great difference in the frequency of duct papillomatosis in the two types of material under analysis when equivalent age-groups are considered. The somewhat higher figure, 36 per cent for duct papillomatosis in the entire series of 300 cancerous breasts against the figure 29 per cent for 200 noncancerous breasts is, likewise, not of sufficient degree to indicate more than a trend.

If no impressive difference in frequency, then, is there a difference in the kind of papillomatosis? This may be ascertained from the following comparisons.

1 Are macroscopic papillomas more common to one group than the other? Analysis shows that of the 58 benign breasts with papillomas, 14, or 26 per cent, were greater than 1 mm in diameter. Of these 14 cases of macroscopic papillomas, six showed additional foci of microscopic papillomatosis. Of the 108 cancerous breasts with papillomas only eight, or 7 per cent, were macroscopic, and in each of these eight cases additional foci of microscopic papillomatosis were found. These findings are not startling, and can be summarized by stating that macroscopic papillomas are more characteristic of benign than cancerous breasts, and that "solitary" macroscopic papillomas are decidedly accented in this group. In passing, it can be said that the bulk of the macroscopic papillomas falls between the ages 50-60, but extremes below 30 and beyond 60 occur.

2 Is there a difference in the "degree" of the papillomatosis of cancerous and noncancerous breasts? The term "degree" is used here to designate the multiplicity of the lesions and is qualified by the relative terms marked, moderate and slight.

TABLE VII
DEGREE OF PAPILLOMATOSIS

	Slight	Moderate	Marked
Noncancer group (58)	31, or 53%	16 or 27%	11 or 20%
Cancer group (108)	69 or 64%	27 or 25%	12 or 11%

Again, nothing very impressive is seen in the comparative figures. The above grouping by "degree" does not take into special account the minute histology of the single cells.

3 Are the papillary lesions of one group more or less apt to be atypical, histologically, than in the other? The term "atypical" here indicates a disturbance in cell uniformity and includes the usual traits such as altered stainability, variation in size and/or shape, and loss of polarity. All of these characters are subject to much variation ranging from trivial alteration to a stage where they merge imperceptibly with the histology of cancer. When a case is called "atypical" it signifies that it is at least of a certain substantial level of atypism. No effort is made to classify beyond this arbitrary line. In the 58 cases of papillomatosis from noncancerous breasts only five were considered atypical while in the 108 cancer-containing breasts, the papillomatosis was considered atypical in 45. It is emphasized that the lesions

were not part of a cancer. The far higher incidence of atypical papillomatosis in cancerous breasts is one of the few outstanding differences recorded in this comparative study. It is a qualitative difference about five times more common in cancer-containing breasts. The contrast is made more obvious by recalling that orderly papillomatosis is almost as common in one type of material as the other.

Table VIII shows the lesions that occur in unison with papillomatosis. For purposes of comparison the table includes the absolute frequency of the same lesions as they occurred in the two groups as a whole.

TABLE VIII
LESIONS ACCOMPANYING DUCT PAPILLOMATOSIS

	58 Noncancer Cases with Duct Papillomatosis	200 Consecutive Noncancer Cases	108 Cancer Cases with Duct Papillomatosis	300 Consecu- tive Cancer Cases
--	---	---------------------------------------	---	--------------------------------------

1	Hyperplasia of duct epithelium	90%	39%	95%	57%
2	Intracystic papilloma	4%	2%	1%	1%
3	Blunt duct adenosis	62%	26%	49%	26%
4	Apocrine epithelium	63%	42%	50%	39%
5	Sclerosing adenosis				
	A Diffuse	2%	1.5%	1%	0.3%
	B Focal	16%	11%	13%	7%
6	Fibro adenoma	8%	19%	4%	7%
7	Tendency to fibro adenoma	10%	3%	4%	6%
8	Cysts	74%	53%	32%	27%
9	Stasis and distension of ducts	56%	34%	53%	42%
10	Duct metaplasia	48%	34%	64%	45%
11	Periductal mastitis	36%	22%	16%	14%
12	Fat necrosis	0	2%	1%	1.3%
13	Lobule frequency				
	Numerous	12%	13%	10%	10%
	Average	62%	61%	40%	35%
	Few	26%	26%	50%	55%
14	Periductal myoid atrophy	54%	27%	52%	42%

The percentage differences are nowhere great enough to show any fundamental difference in the lesions that accompany papillomatosis in cancerous as opposed to noncancerous breasts—at least no difference that is not manifest in these two groups taken as a whole. It is of distinct interest to note again the tendency of certain cystic and proliferative lesions to occur in unison—cysts, hyperplasia of duct epithelium, duct papillomatosis, blunt duct adenosis, apocrine epithelium and sclerosing adenosis. Each of these lesions has been, or will, be discussed from the point of view of what morphologic part they seem to play in mammary carcinogenesis. Attention is called, again, to the failure of fibro-adenoma, another proliferative lesion, to be found concomitantly with the other lesions just mentioned, further suggesting that fibro-adenoma is a different proliferative manifestation. In the section on cysts, factors influencing the frequency of periductal mastitis and associated lesions have been mentioned, and no further comment will be made until this group is separately dealt with.

A further means of comparing the cancerous and noncancerous series is afforded by tabulating the preceding group of 14 lesions as they occur in the absence of duct papillomatosis.

CANCEROUS VS NONCANCEROUS BREASTS

TABLE IX

COMPARATIVE FINDINGS IN BREASTS WITH AND WITHOUT DUCT PAPILLOMATOSIS

	58 Noncancer Cases with Duct Papillomatosis	142 Noncancer Cases without Duct Papillomatosis	108 Cancer Cases, with Duct Papillomatosis	192 Cancer Cases without Duct Papillomatosis
1 Hyperplasia of duct epithelium	90%	23%	95%	35%
2 Intracystic papilloma	4%	1%	1%	1.5%
3 Blunt duct adenosis	62%	14%	49%	13%
4 Apocrine epithelium	63%	35%	50%	33%
5 Sclerosing adenosis				
A Diffuse	2%	1%	1%	0.5%
B Focal	16%	11%	13%	3%
6 Fibro adenoma	8%	23%	4%	9%
7 Tendency to fibro adenoma	10%	3%	4%	7%
8 Cysts	74%	44%	32%	25%
9 Stasis and distention of ducts	56%	27%	53%	36%
10 Duct metaplasia	48%	28%	64%	34%
11 Periductal mastitis	36%	17%	16%	13%
12 Fat necrosis	0	3%	1%	1.5%
13 Lobule frequency				
Numerous	12%	13%	10%	10%
Average	62%	67%	40%	33%
Few	26%	27%	50%	57%
14 Periductal myoid atrophy	54%	17%	52%	36%

In Table IX the same trends as formerly noted are repeated in sharper contrast. Regardless of whether breasts do or do not contain a cancer, they tend to maintain similar structure when cross-examined on the basis of possessing a common histologic factor such as presence or absence of duct papillomatosis. As the noncancerous proliferative lesions of cancerous breasts are analyzed, it begins to be apparent that the pattern of the breast tissue is more influenced by the presence or absence of these noncancerous lesions than by the presence of the cancer itself.

The direct part played by duct papillomatosis in the morphogenesis of cancer of the breast cannot be stated in very exact terms. In contrast to cysts and other common lesions, however, there is ample evidence of a far more direct relationship. In the 300 mammary carcinomas studied here, there were 45 examples of atypical papillary hyperplasia with various degrees of change bordering on the histology of cancer. In over one-half of the 300 cancers, there was evidence of duct origin represented by papillary or stratified intraductal foci of tumor. In the remainder of these mammary carcinomas the duct origin could not be satisfactorily traced, but by far the greatest number had the histologic traits usually seen in infiltrating duct carcinoma. In a small number of cases, lobule origin was apparent (about one in 25), and in still another small group simultaneous duct and lobule participation seemed present. The traceability of mammary cancer to any structure but the mammary ducts is uncommon, so that any theory of carcinogenesis in the human female breast must necessarily concern itself principally with lesions of the duct system. The commonest abnormality of the duct epithelium is papillary or near-papillary hyperplasia, and every conceivable transition can be noted to *in situ* or infiltrating cancer. Since the

usual mammary carcinoma is fully developed and advanced when it comes under observation no one can say what percentage of these cancers develops on a basis of papillomatosis, but it can be said that this basis does exist for some of the cases, and it is rare to find any early duct cancer of the breast in the absence of atypical papillomatosis.

The fact previously noted that atypical papillomatosis is seldom seen in noncancerous breasts is the only impressive difference shown so far. The actual number of papillary lesions that eventually become mammary cancers must necessarily be a very minute fraction, and we know of no way at the present to prognosticate the probable course of any given histologic type. It is certain that most of these lesions disappear from the breast, and in the material studied here there are many examples of the retrograde phases of these lesions, namely, varying degrees of abortive fibrosis with gradual obliteration of epithelial component. Now and then, however, one will find an area of papillomatosis in which the hyalinosis is apparently interrupted by a new surge of epithelial hyperplasia which may or may not show histologic atypism. This observation prompted the query as to whether or not a characteristic of cancerous breasts was persistence of papillary lesions. This is answered in the negative by noting that both noncancerous and cancerous breasts between ages 40-50 have papillary lesions in the same frequency—40 per cent, and the corresponding figures for the ages 50-60 are 23 per cent for noncancerous and 28 per cent for cancerous breasts. In the noncancer group the 58 cases of papilloma included five that were histologically atypical. This number is entirely too few to ascertain if age influences atypicalness, and no conclusion can be drawn from their occurrence at ages 48, 43, 55, 41 and 46. In the cancer cases with atypical papillomatosis, the age curve is practically identical with the age curve of the cancer cases with nonatypical papillomatosis, and in addition the same age curve is followed by the non-atypical papillomatosis of the noncancer series of cases.

To illustrate transitions from orderly duct papillomatosis to mammary carcinoma is not difficult if samples are selected from several cases, but the entire gamut of alteration occurs only in the exceptional single case. Such a case with step-like histologic sequences is shown in Figures 1 through 8.

IV — BLUNT DUCT ADENOSIS

Blunt duct adenosis is a term we have used to designate one of the common proliferative lesions of the breast. Although it is undesirable to invent new terms, nevertheless, this designation expresses the principal characteristic of these structures, namely, that they are ducts which end abruptly and do not terminate in lobules. The origin, course and termination of these blunt end ducts can be traced easily in serial sections. It was after this sort of study that it became obvious that one cannot rely upon a single microscopic section in deciding whether a given structure is a minute cyst or not, hence the limiting of tabulation of cysts in this paper to cysts of

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macroscopic proportion Blunt end ducts usually originate at the distal or near distal extremities of the duct system, and since they begin at a point where periductal myoid tissue is absent or markedly attenuated, they typically lack this myoid investment and have a relatively poorly developed

Fig 1

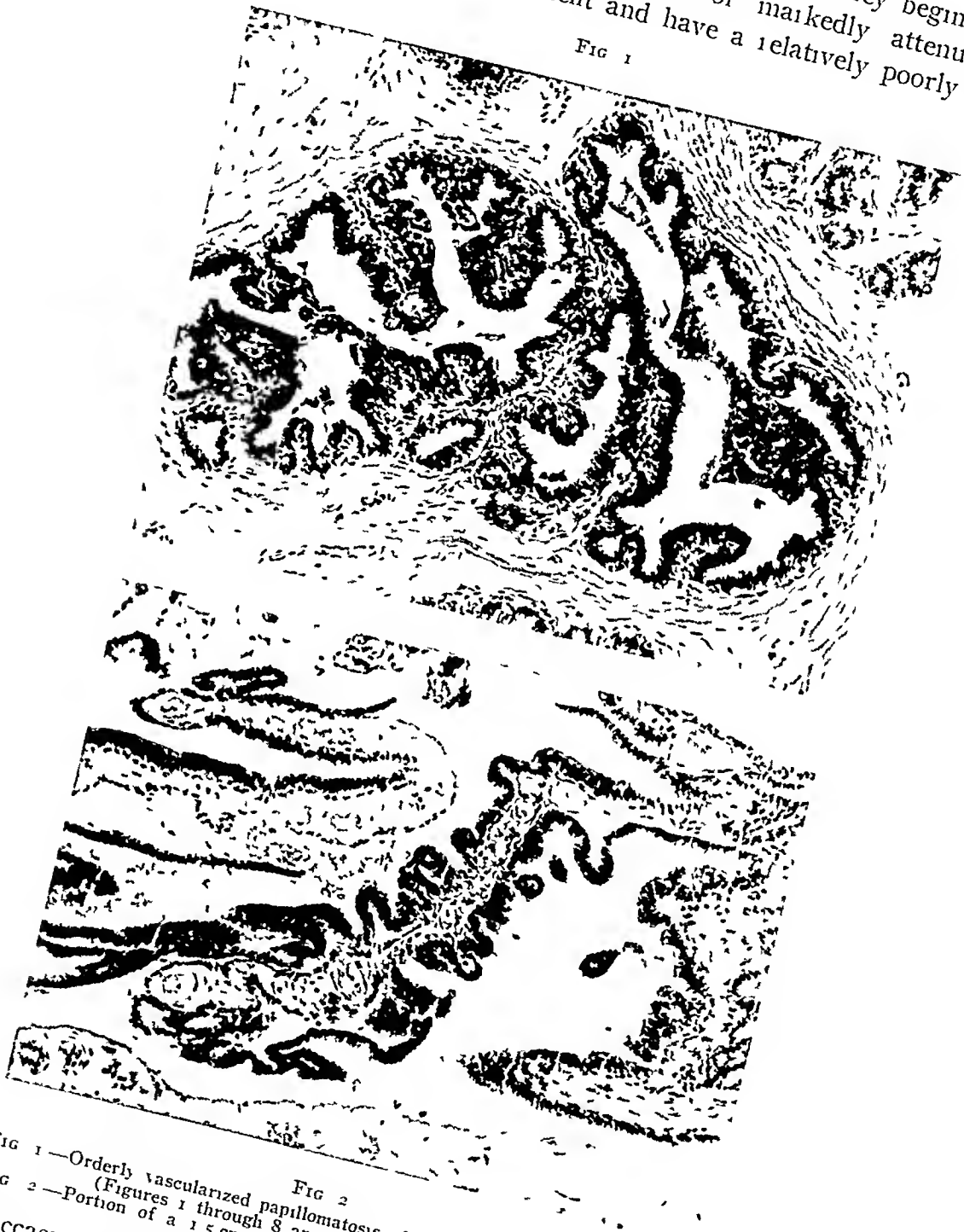


Fig 1—Orderly vascularized papillomatosis of medium sized mammary ducts
(Figures 1 through 8 are taken from a single breast)
Fig 2—Portion of a 1.5 cm papilloma in a large duct Orderly structure

On occasions this myoid element is seen at or near the main stem of a "parent" blunt duct, but it invariably disappears within a space of a millimeter The elastica in the walls of these ducts is quite variable in amount, but commonly one sees in the breast tissue adjacent, an apparent

condensation of extraductal elastica. The initial branch of a blunt end duct may not divide, but ordinarily one and often many subdivisions are encountered in serial sections. They are apt to end in a cluster of closely but irregularly spaced blind channels but with no resemblance to usual lobule formation. It is to be noted that these structures have long since lost their

FIG 3



FIG 4

FIG 3—Less orderly papillary and partly solid hyperplasia. Not vascularized.
FIG 4—Nonvascular stratification and papillary piling up. Cytology atypical.

myoid envelope, whereas in the mammary lobules it is common for the terminal duct to retain its myoid layer until or even after it enters the lobule. The blunt end ducts furthermore often have relatively wide lumina which are actually wider by far than the mammary ducts from which they sprouted. The epithelial lining of these ducts is by no means uniform and

is apt to vary from point to point in any given duct or its divisions. Sometimes there is a two-layered epithelial lining with a low or flat basal row and an outer row that varies from low to quite tall cylindrical. Often the inner row of cells extrudes from its distal border a pink, homogeneous "cytoplasmic prolongation" identical with what is often seen protruding from

FIG 5

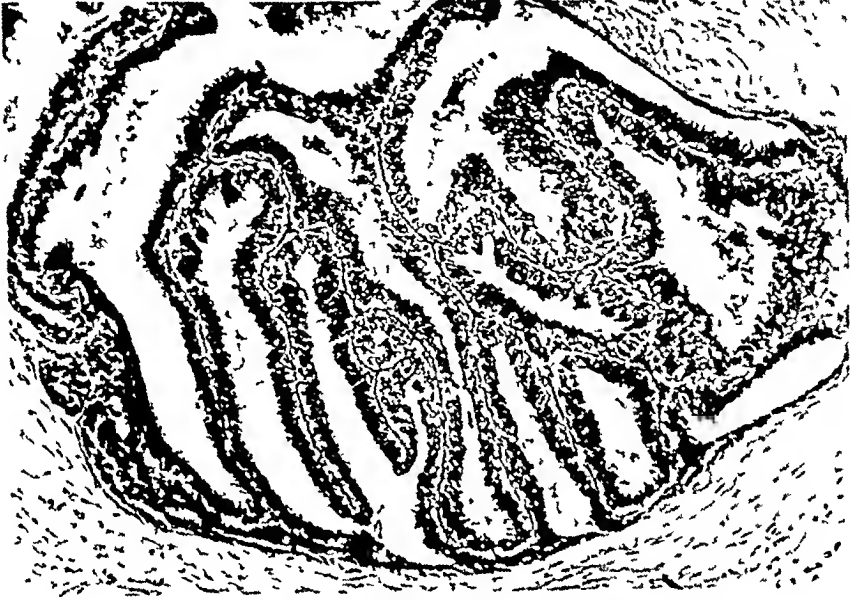


FIG 6

FIG 5—Intraductal papilloma cytologically rather uniform except at left lower corner. Over all pattern atypical in spite of dominant maintenance of polarity.

FIG 6—Distinctly more advanced alteration of same general pattern as Figure 5. Low grade intraductal papillary carcinoma.

the cells of normal mammary ducts. In addition to the relatively orderly epithelial lining just mentioned all degrees of stratification continuing to papillomatosis appear, and are by no means uncommon. It is not very unusual to find apocrine metaplasia of the epithelial lining of blunt end ducts. Finally,

blunt end ducts may have a single low or flat row of epithelium. The variable structure of blunt end ducts seems in all likelihood referable to whether the process is seen in an early or late phase. The early lesions have relatively narrow lumina with taller lining cells while the later lesions show broader lumina and shorter lining cells. Mitoses are uncommon but far more apt

FIG 7

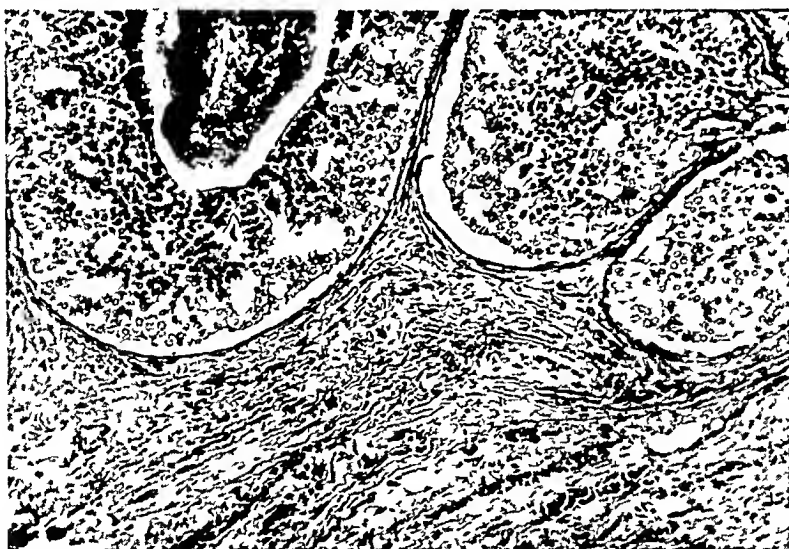
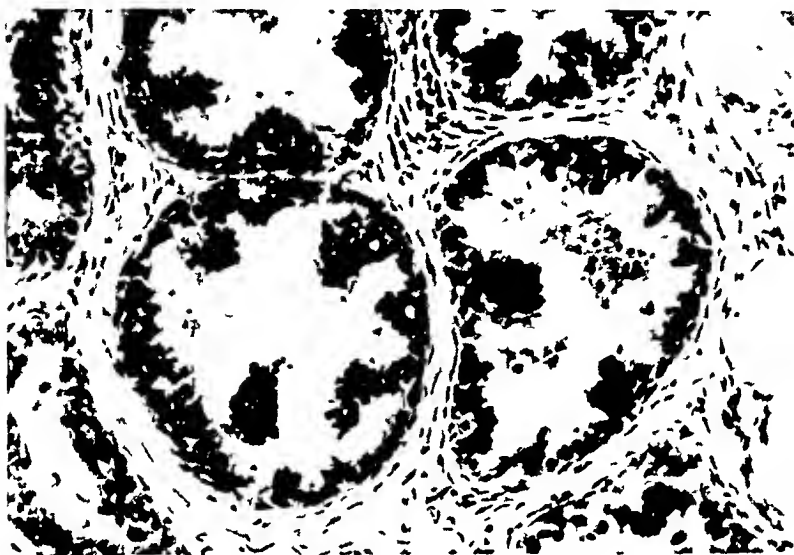


FIG 8

FIG 7—Papillary intraductal carcinoma
FIG 8—Fully developed intraductal and infiltrating carcinoma

to occur in the earlier proliferative phases. In a single breast, blunt end ducts of every phase may be found, as if the organ had responded to multiple periods of stimulation alternating with periods of quiescence. The very late phases of great dilatation and flattening of epithelium practically never show any sign of proliferation. The degree of blunt duct adenosis ranges

from an occasional focus to a level where almost all of a several centimeter mass of breast tissue may be made up principally of these structures. In such a marked case, two findings stand out. There are practically no lobules, and small- (1-2 Mm) and medium- (1 cm) sized cysts are very numerous. This supports the idea of an origin of blunt end ducts from terminal ducts, with subsequent lobule obliteration as the dilatation progressively involves the preexisting lobules. It further suggests that cyst formation may be an end-result of blunt duct adenosis. Finally, the smallest cysts one sees invariably fail to have a circumferential layer of myoid.

In the 200 noncancerous breasts blunt duct adenosis was seen in 52, or 26 per cent, and in the 300 cases of mammary cancer, the figures are 78, or 26 per cent. By decades the occurrence is as shown in Table X.

TABLE X
OCCURRENCE OF BLUNT DUCT ADENOSIS

Decade	Noncancer Cases	Cancer Cases
30-40	36%	28%
40-50	28%	45%
50-60	20%	13%

The divergence in the frequency of blunt duct adenosis in the decade 40-50 is the greatest shown. A possible explanation for this is presented in the following. It has been previously shown in the decade 40-50 that cysts occurred in 65 per cent of noncancerous breasts and in only 18 per cent of cancerous breasts. It also seems, on the basis of preceding morphologic observation, that blunt duct adenosis is apt to eventuate in cyst formation. Hence, one may suggest that for the decade 40-50 the tendency in the benign cases is toward cyst formation with partial obliteration of the structures from which they arose. Consequently, there is a relative diminution of these antecedent structures in the age-period when cysts are most common. Similarly, in the decade 40-50 the tendency in the cancer cases is away from cyst formation, and this results in a greater relative frequency of the antecedent structures in the age-period when cysts are relatively fewest. It is, likewise, apparent that these blunt end ducts become less frequent with advancing age, hence sharing in the general tendency toward atrophy of the mammary system.

Table XI enumerates the lesions that accompany blunt duct adenosis. As in preceding tables, the frequency of these lesions as they occur in the cancer and noncancer groups as a whole is represented.

Quantitative differences again are shown and particularly noticeable is the marked tendency for the previously designated cystic and proliferative lesions to occur simultaneously, namely, cysts, hyperplasia of duct epithelium, duct papillomatosis, blunt duct adenosis, apocrine epithelium and sclerosing adenosis. Emphatically presented, again, is the failure of fibro-adenoma to be accented with this group. No differential feature between cancerous and noncancerous breasts appears that is not explainable by the preliminary comparisons of these types of breasts in various age groups.

TABLE XI
LESIONS ACCOMPANYING BLUNT DUCT ADENOSIS

	52 Noncancer Cases with Blunt Duct Adenosis	200 Consecu- tive Non- cancer Cases	78 Cancer Cases with Blunt Duct Adenosis	300 Consecu- tive Cancer Cases
1 Hyperplasia of duct epithelium	77%	39%	84%	57%
2 Duct papillomatosis	60%	29%	61%	36%
3 Intracystic papilloma	Not charted	2%	Not charted	1%
4 Apocrine epithelium	63%	42%	53%	39%
5 Sclerosing adenosis				
A Diffuse	2%	1 5%	1%	0 3%
B Focal	27%	11%	14%	7%
6 Fibro adenoma	14%	19%	6 5%	7%
7 Tendency to fibro adenoma	13%	3%	6 5%	6%
8 Cysts	87%	53%	44%	27%
9 Stasis and distention of ducts	40%	36%	53%	42%
10 Duct metaplasia	50%	34%	74%	45%
11 Periductal mastitis	30%	22%	15%	14%
12 Fat necrosis	0	2%	0	1 3%
13 Lobule frequency				
Numerous	11%	13%	14%	10%
Average	68%	61%	41%	35%
Few	21%	26%	45%	55%
14 Periductal myoid atrophy	37%	27%	50%	42%

A further means of cross-analysis is afforded by comparing the cancer and noncancer breasts that show blunt duct adenosis with those that do not

TABLE XII
COMPARATIVE FINDINGS IN BREASTS WITH AND WITHOUT BLUNT DUCT ADENOSIS

	52 Noncancer Cases with Blunt Duct Adenosis	148 Noncancer Cases without Blunt Duct Adenosis	78 Cancer Cases with Blunt Duct Adenosis	222 Cancer Cases without Blunt Duct Adenosis
1 Hyperplasia of duct epithelium	77%	25%	84%	47%
2 Duct papillomatosis	60%	18%	61%	28%
3 Intracystic papilloma	Not charted		Not charted	
4 Apocrine epithelium	63%	34%	53%	34%
5 Sclerosing adenosis				
A Diffuse	2%	1 5%	1%	0 5%
B Focal	27%	7%	14%	4%
6 Fibro adenoma	14%	21%	6 5%	9%
7 Tendency to fibro-adenoma	13%	2%	6 5%	5%
8 Cysts	87%	41%	44%	21%
9 Stasis and distention of ducts	40%	33%	53%	40%
10 Duct metaplasia	50%	30%	74%	36%
11 Periductal mastitis	30%	18%	15%	14%
12 Fat necrosis	0	3%	0	2%
13 Lobule frequency				
Numerous	11%	13%	14%	9%
Average	68%	57%	41%	33%
Few	21%	30%	45%	58%
14 Atrophy of periductal myoid	37%	24%	50%	39%

The same trends seen in Table XII are repeated in sharper contrast with the accent still on the simultaneous occurrence of the lesions already designated

Blunt duct adenosis cannot be associated with pregnancy or nursing, inasmuch, as these states were equally common in the cases with or without this lesion and, further, blunt duct adenosis is seen in individuals who have

CANCEROUS VS NONCANCEROUS BREASTS

never been pregnant Finally, these structures show no relation to the phasic changes of the menstrual cycle They are, undoubtedly, proliferative manifestations and they apparently can exist for considerable periods, eventuate in cyst formation, or undergo involution and atrophy

FIG 9



FIG 9 —Relatively early phase of blunt duct adenosis Failure of normal lobule formation
FIG 10 —Process of blunt duct adenosis more fully developed

It is difficult to be sure of the part blunt end ducts play in the morphogenesis of mammary carcinoma Papillomatosis occurs in blunt end ducts but it is not as common as in the permanent duct system and is far less liable to show histologic atypism Any duct that is the site of papillomatosis is very

likely to show atrophy of its periductal myoid layer and, since absence of myoid is a prime characteristic of blunt end ducts, there are many occasions when one is uncertain whether to call a papilloma-containing duct a permanent duct or a newly formed blunt end duct. We were able to trace cancer to

FIG 11



FIG 12

FIG 11—Papillomatosis in a group of blunt end ducts
FIG 12—Intermediate phase of blunt duct adenosis. Subsidence of proliferative impulse, widening of lumina

this source with reasonable certainty in only four out of 300 cases, which is in all probability a somewhat low figure. Some of the principal structural traits of blunt duct adenosis are represented in Figures 9 through 13

V APOCRINE EPITHELIUM

This term refers to epithelium consisting of the very characteristic large, usually tall, cylindrical cells that have relatively small nuclei and abundant,

clear, bright, eosinophilic cytoplasm. Aggregates of this kind of epithelium can commonly be seen in the gross as discrete yellowish-brown, slightly elevated, glistening areas, usually 1-2 Mm in diameter but occasionally of much larger dimension. The larger aggregates are almost invariably partly cystic

FIG 13



FIG 14

FIG 13—Late phase of blunt duct adenosis
FIG 14—Apocrine epithelium in papillary form. Cytology not atypical
(Figures 14 through 17 were taken from a single breast)

and/or adenomatoid. Microscopically, in single sections, apocrine epithelial islands may be seen as apparently isolated glandular or cystic structures or, less often, they are seen in direct continuity with a mammary duct that is lined elsewhere by conventional epithelium. When examined in serial

sections, it is surprising how often a connection with ducts or lobules is demonstrated, and it becomes evident that this is the usual structural relationship. Complete isolation from the duct system is shown on occasion and when this is true, cystic distention is the rule. Papillary hyperplasia of slight or moderate degree is rather common appearing in about a third of apocrine epithelial foci of both cancerous and noncancerous breasts.

Some form of apocrine epithelium was seen in 42 per cent of breasts free from cancer, and in 39 per cent of breasts containing cancer. Most of these findings are based on microscopic study and, hence, are largely chance observations. The frequency would of course be greater if very numerous blocks were made, and we can only regard the figures given here as comparative and not absolute. Table XIII shows the incidence by decades.

TABLE XIII
OCCURRENCE OF APOCRINE EPITHELIUM

Decade	Noncancer Cases	Cancer Cases
30-40	33%	25%
40-50	47%	44%
50-60	40%	31%

Thus, no wide divergence can be demonstrated between cancer and noncancer cases. It is worth noting, however, that these structures are most frequent during the decade 40-50, when the breast shows its highest level of noncancerous proliferative lesions. Without the series of noncancerous breasts as a control group, the common occurrence of this kind of epithelium in cancer cases might be interpreted as being important in mammary carcinogenesis, especially by those who claim that a high proportion of breast cancers are of sweat gland origin, which viewpoint we emphatically reject. The same is equally true of other lesions but it is our desire to show that mere statistical association needs the support of demonstrable morphologic relationship before any given lesion can be ascribed a place of importance in the actual histogenesis of cancer. Pursuing this course as regards apocrine epithelium, it was possible to designate only three mammary cancers in 300 as showing histologic characters that would prove or suggest origin from this source. Furthermore, it is difficult to find in either cancerous or noncancerous breasts any foci of apocrine epithelium that show histologic atypism. In the 500 cases studied here, only two examples of this change were found. Both of these atypical foci were papillary and in each case the breast contained a cancer. One of these was an infiltrating duct carcinoma of usual type and the other a carcinoma with quite large cylindrical cells having relatively small nuclei and abundant clear, eosinophilic cytoplasm. In a large series of mammary cancers about 3 per cent are composed of cells resembling the apocrine type. There is then no way of ascribing a major morphologic rôle to these cells in mammary carcinogenesis. It is not possible to detect transitions from mammary apocrine epithelium to mammary cancer in any but the very exceptional case. Such a sequence is shown in Figures

CANCEROUS VS NONCANCEROUS BREASTS

Fig 17

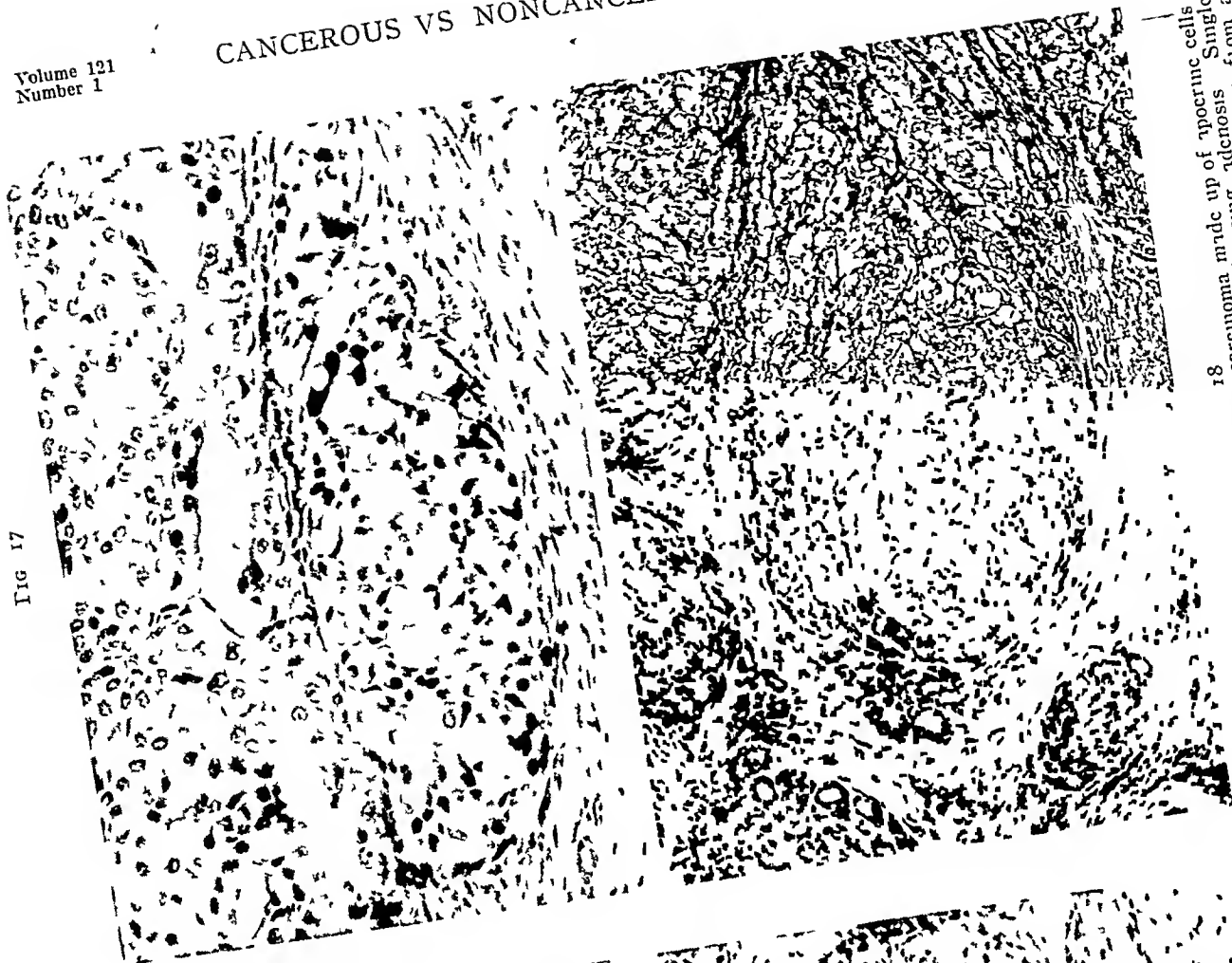


Fig 18

Fig 17--Intraductal and infiltrating carcinoma made up of apocrine cells
Fig 18--Highly cellular, florid phase of sclerosing adenosis. Section from a field of type commonly confused with mammary carcinoma discrete 2.5 cm mass

Fig 15

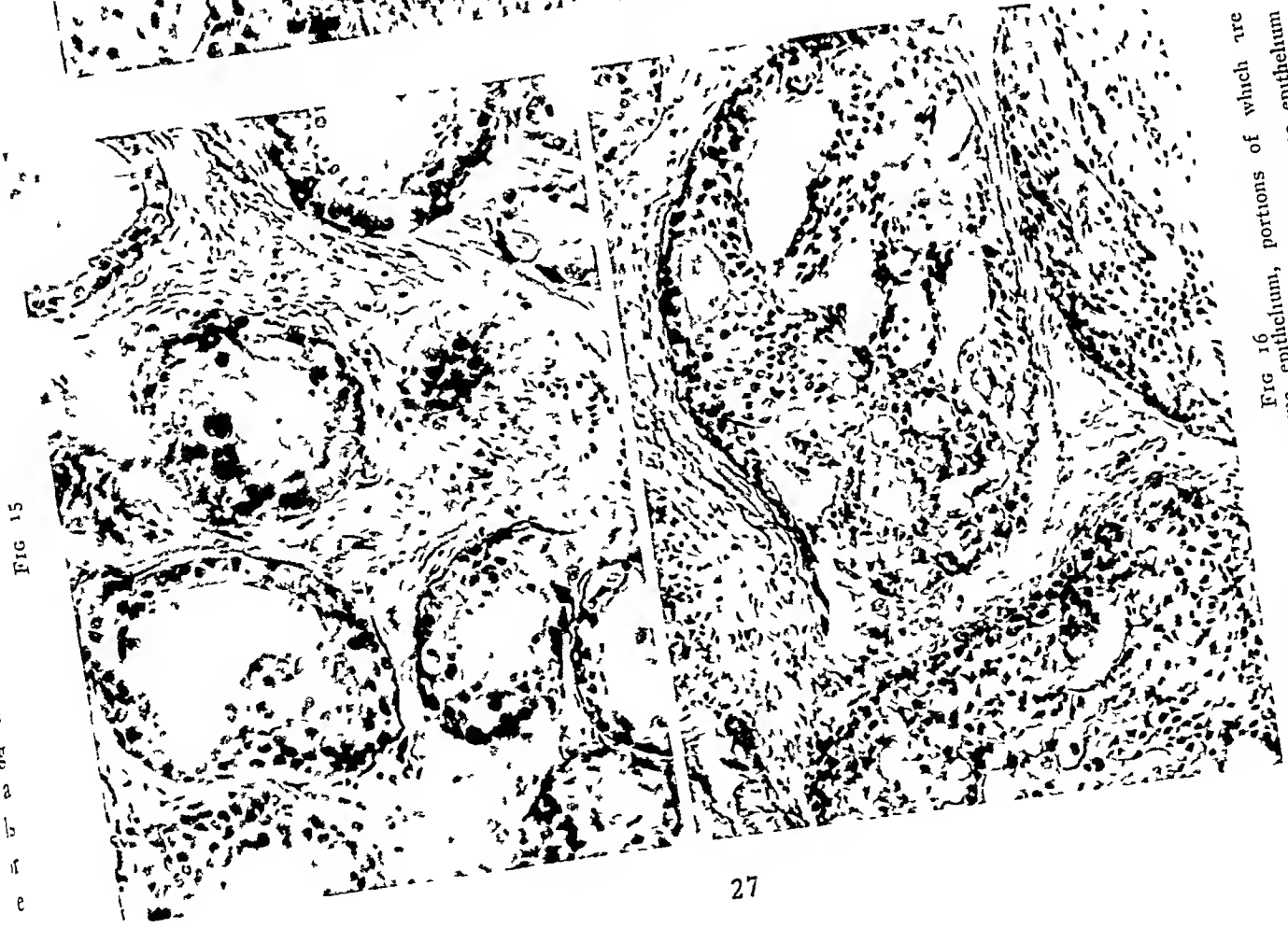


Fig 16--Noninfiltrating carcinoma composed of apocrine epithelium
Fig 15--Ducts lined by apocrine epithelium, portions of which are of atypical structure
Fig 16--Noninfiltrating carcinoma composed of apocrine epithelium

14 through 17, the illustrations being taken from a single breast. All the epithelium shown had the characteristic eosinophilic tinctorial quality. Axillary nodes were involved in this case.

Table XIV is designed to show what lesions are apt to occur in cancerous and noncancerous breasts when the common factor is the presence of apocrine epithelium. As usual, the occurrence of these lesions in the 200 benign breasts and 300 cancerous breasts, as a whole, is included.

TABLE XIV
LESIONS ACCOMPANYING APOCRINE EPITHELIUM

	84 Noncancer Cases, with Apocrine Epithelium	200 Noncancer Cases	117 Cancer Cases with Apocrine Epithelium	300 Cancer Cases
1 Hyperplasia of duct epithelium	65%	39%	70%	57%
2 Duct papillomatosis	45%	29%	45%	36%
3 Intracystic papilloma	0	2%	1%	1%
4 Blunt duct adenosis	56%	26%	47%	26%
5 Sclerosing adenosis				
A Diffuse	1%	1.5%	0	0.3%
B Focal	23%	11%	14%	7%
6 Fibro adenoma	8%	19%	6%	7%
7 Tendency to fibro adenoma	4%	3%	8%	6%
8 Cysts	83%	53%	40%	27%
9 Stasis and distention of ducts	50%	36%	62%	42%
10 Duct metaplasia	52%	34%	71%	45%
11 Periductal mastitis	30%	22%	20%	14%
12 Fat necrosis	0	2%	2%	1.3%
13 Lobule frequency				
Numerous	10%	13%	7%	10%
Average	59%	61%	39%	35%
Few	31%	26%	54%	55%
14 Periductal myoid atrophy	37%	27%	45%	42%

TABLE XV
COMPARATIVE FINDINGS IN BREASTS WITH AND WITHOUT APOCRINE EPITHELIUM

	84 Noncancer Cases with Apocrine Epithelium	116 Noncancer Cases without Apocrine Epithelium	117 Cancer Cases with Apocrine Epithelium	183 Cancer Cases without Apocrine Epithelium
1 Hyperplasia of duct epithelium	65%	19%	70%	42%
2 Duct papillomatosis	45%	24%	45%	30%
3 Intracystic papilloma	0	3%	1%	2%
4 Blunt duct adenosis	56%	4%	47%	12%
5 Sclerosing adenosis				
A Diffuse	1%	2%	0	2%
B Focal	23%	5%	14%	2%
6 Fibro adenoma	8%	27%	6%	8%
7 Tendency to fibro adenoma	4%	6%	8%	4%
8 Cysts	83%	31%	40%	19%
9 Stasis and distention of ducts	50%	25%	62%	30%
10 Duct metaplasia	52%	22%	71%	30%
11 Periductal mastitis	30%	16%	20%	11%
12 Fat necrosis	0	3%	2%	1%
13 Lobule frequency				
Numerous	10%	14%	7%	13%
Average	59%	59%	39%	32%
Few	31%	27%	54%	55%
14 Periductal myoid atrophy	37%	20%	45%	39%

The trends shown in previous tables are repeated in Table XIV, and in Table XV a further comparison is shown by charting the lesions occurring in breasts that do and do not contain apocrine epithelium

Study of the preceding tables justifies the statement that apocrine epithelium is most apt to be found in a breast containing certain noncancerous proliferative lesions. This is further supported by the following. Rather commonly in cases of papillomatosis, isolated foci of apocrine cells or glands are seen in that part of the papilloma which protrudes into the duct lumen. These foci are often multiple and are entirely separated from one another, so that it seems reasonable under these circumstances to regard them as metaplastic in nature, newly formed, and, therefore, proliferative. It can also be shown that apocrine elements take part in sclerosing adenosis and blunt duct adenosis, the component parts of which are certainly newly formed structures. Occasional mitoses may be found in areas of epithelium of apocrine pattern, indicating that these are in some instances at least proliferative rather than static structures. We believe that all "pink epithelium" in the breast arises on a basis of hyperplasia and metaplasia. Absolute determination of this would depend on studying material from breasts of gradually decreasing age-groups until the earliest manifestations are encountered. We have seen apocrine elements in a breast of an infant a few months old. This was, however, in an actively proliferative adenomatoid lesion of papillary character.

In summary, an analysis of cancerous and noncancerous breasts, using the presence or absence of apocrine epithelium as the means of comparison, shows no essential difference.

VI SCLEROSING ADENOSIS

The terms "fibrosing adenomatosis," "sclerosing adenomatosis" and "sclerosing adenosis" have long been used interchangeably in this Hospital to identify a specific lesion quite commonly misinterpreted and erroneously diagnosed as mammary carcinoma. The interchangeable terms above are incompletely descriptive since they designate only one phase of the process to be described here, namely, that of sclerosis. These lesions have been also termed "myo-epithelial" tumors¹. The phase of fibrous sclerosis, however, is the one usually seen, it is quite characteristic, and hence it seems permissible to stress this feature in selecting a term applicable to the lesion. The stage of fibrous sclerosis is, of course, a late one and it is not usual to see the earlier or "florid" phase of pure epithelial efflorescence. So far, we have seen only a single case in which the microscopic structure was purely "florid." It is rare to find "floridness" the chief feature in any case, but over a period of some years all conceivable intermixtures of florid areas and sclerosing areas have been observed.

Sclerosing adenosis occurs in two forms. In the first of these a palpable tumor mass is present. In the second, minute focal areas are seen only on microscopic examination and the lesions are but incidental findings. The

focal microscopic lesions are 20 to 30 times as frequent as the discrete tumors, and present no clinical problem

When sclerosing adenosis presents as a palpable lump the true identity of the process can be established by the following characters. The lump is freely movable in the breast and there are no secondary skin changes. The patients are usually in the twenties or thirties. We have seen no case below puberty and only a few in the teens. Now and then the lesion occurs after forty and in isolated instances in the fifties and sixties. The tumors are customarily seen by the pathologist when a specimen is locally excised and submitted for frozen-section, the clinical diagnosis having been fibroadenoma or cyst. The consistency is ordinarily less rubbery than in fibroadenoma and less firm than in mammary carcinoma. However, both extremes are possible. The tumors lack the smooth globoid or elliptical shape of a fibroadenoma and instead show nodularity of varying coarseness. They are discrete but are apt to be indefinitely encapsulated. On section, resistance to cutting is variable, depending on elasticity or firmness. The cut surface is grayish-white as a rule but may be partly or chiefly faint, pinkish-yellow. Usually, the chalky streaks so common in mammary cancer are absent but in several instances they have been observed. The most important gross observation is the detection of usually definite lobulation that may vary from a millimeter to over a centimeter. The lobulations are chiefly in direct contiguity but they may merge imperceptibly or sometimes be separated by an interval of a few millimeters. There is often a certain minor degree of translucence. The lobulated surfaces customarily project slightly. The periphery of the tumor is characteristically noninfiltrating in appearance but some specimens may be confusing in this respect. Given a case in which there is distinct lobulation, neat circumscription and an absence of chalk streaks a gross diagnosis of cancer is unlikely. But there are a few cases in which lobulation and circumscription are not clear and if chalk streaks and undue firmness are added, one is very apt to get a gross impression of mammary cancer. Fortunately, this combination of characters is rare. If the gross impression of cancer is carried over to the frozen or paraffin section, danger is increased since further microscopic confusion is possible.

The chief pitfall in microscopic diagnosis, particularly in frozen sections, is seeing what superficially appears to be infiltration. When properly analyzed, it becomes evident that this picture is the result of abortive fibrosis or hyalinosis. It is the stage of sclerosis where epithelium has lost the initiative and is "choked" by fibrous or hyaline matrix. This connective tissue dominance produces irregular patterns where thin epithelial columns are haphazardly isolated. Due to constrictive pressure the shape of the epithelial cells is apt to be variable, and the sum total yields an impression of pleomorphism plus invasiveness. It is important to note that, at this phase of the process, nuclear staining is regular and mitoses are absent. Looked at with a low power lens one is often able to detect lobulation even when it is

grossly inconspicuous, and it is usual to find that the greatest degree of sclerosis occurs at the periphery of the lobulated portions. Eventually the entire area of lobulation will become hyalinized, but this is a change that may require many years. In almost any case certain microscopic fields can be found which, if viewed alone, would certainly pass for cancer, and

FIG 19

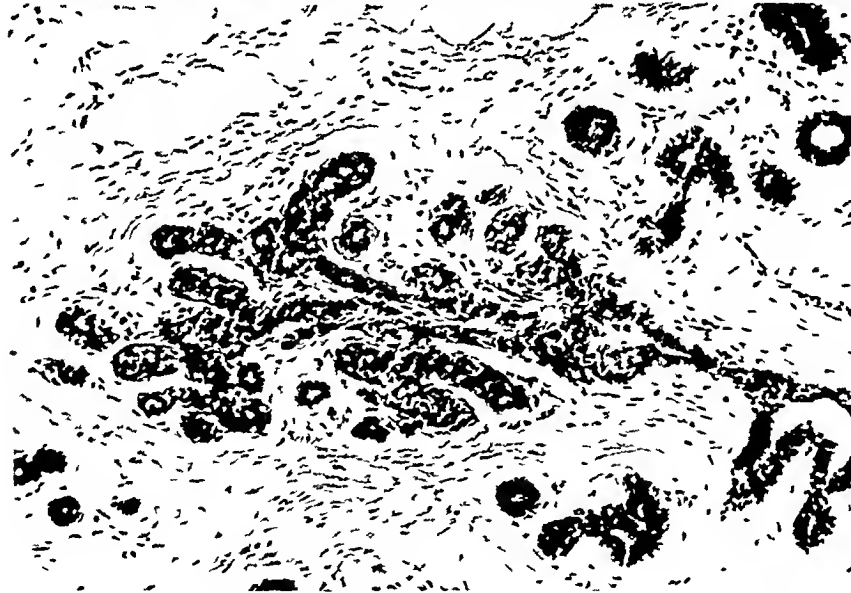
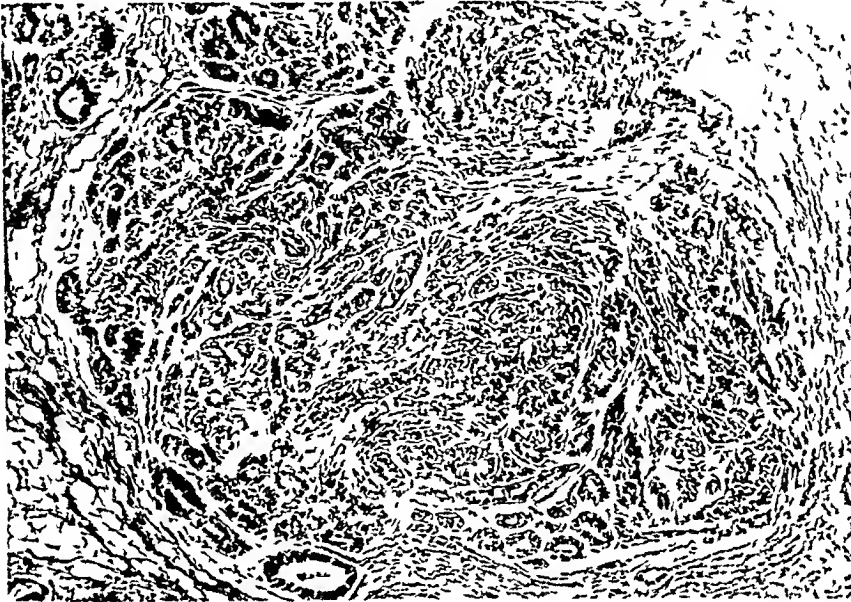


FIG 20

FIG 19 —Section from a palpable mass. Intermediate phase with moderate sclerosis.

FIG 20 —Focal lobular area of sclerosing adenosis. No palpable mass. Beginning sclerosis.

it is necessary that the lesion be examined as a whole and the various changes reconstructed, to insure proper interpretation. The occurrence of cellular areas in these tumors is a further source of microscopic confusion. It has been stated before that florid and sclerosing areas may be present in the same tumor.

During the florid phase moderate cellular variability may be seen and mitoses are not infrequent. These findings must also be discounted and the decision as to diagnosis made on estimating all of the features present. During the florid phase there is extensive multiplication of duct-like structures. Both extra- and intraalobular members of the mammary paren-

FIG 21

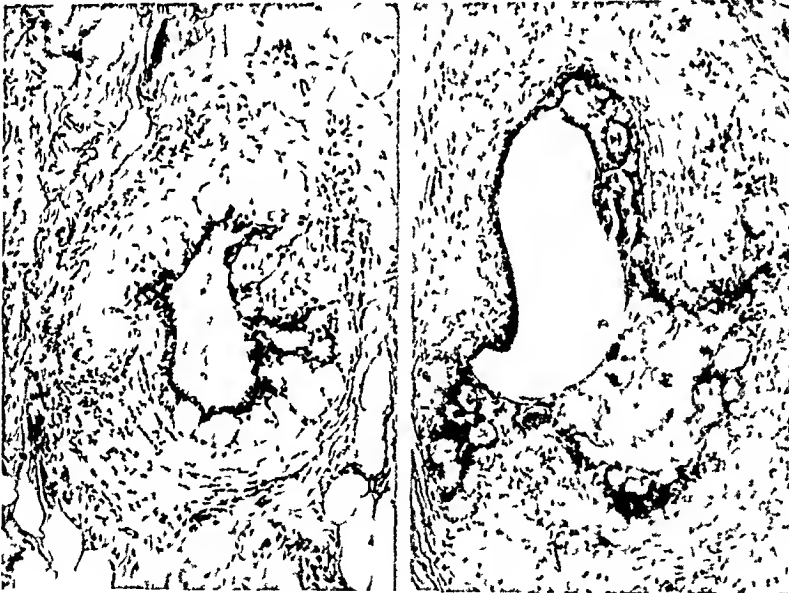
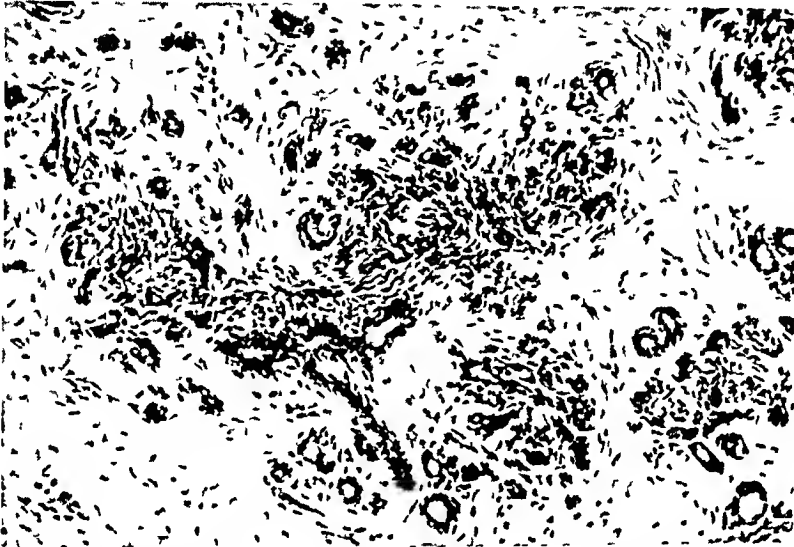


FIG 22

FIG 23

FIG 21—Advanced stage of sclerosing adenosis with obliteration of lumina. No palpable mass.

FIG 22—Dilated mammary duct containing stasis material. Periductal inflammation with infiltrate of lymphocytes and large fat filled phagocytes.

FIG 23—Same process as in Figure 22, but somewhat more advanced.

chyma are seen to participate and the newly formed ducts often show papillary and solid epithelial plugging. Sometimes the proliferation is so diffuse that solid epithelial islands, small and large, are formed in which lumina are not visible, and again single microscopic fields can be found

that would be individually indistinguishable from cancer. In purely florid areas connective tissue does not participate. Even in the florid phase of sclerosing adenosis there is a tendency to lobulation. A generalization may be made that in either phase, the lesion is "put together" in a different fashion than is mammary cancer. Some of the microscopic qualities of sclerosing adenosis are reproduced in Figures 18 through 21.

It seems clear enough that sclerosing adenosis can begin in an intra-lobular position or commence in near-terminal or terminal ducts that fail to form normal mammary lobules. This view of origin is supported by the fact that the newly formed tubular structures practically never have a circumferential myoid investment. When sclerosing adenosis presents as a palpable mass, lobule participation in the tumor proper may not be visible but in outlying breast tissue it is commonly observed. In the focal microscopic form of sclerosing adenosis lobular origin is by far the more common, and often the lesions are of such small proportion that normal lobule size may be maintained, and in some lobules all of the lobule constituents do not necessarily participate. Both florid and sclerosing phases can be seen in the focal microscopic form of sclerosing adenosis, and the only real difference between this form and the tumorous form is that one occurs in miniature.

It may be well to repeat that sclerosing adenosis infrequently produces a palpable tumor. This infrequency is undoubtedly the chief reason that it is so apt to be mistaken for cancer. On a Surgical Service that does over a thousand breast operations yearly, the annual occurrence of the palpable or clinical form of the disease ranges from six to twelve cases.

In the 200 noncancerous cases studied here, three discrete tumors due to sclerosing adenosis were seen, while in the 300 cancer cases, there was only one example, in addition of course, to the cancer. In the statistics to follow, these few instances of discrete tumor cases have been merged with the focal microscopic type. Thus, in 200 breasts without cancer, sclerosing adenosis was found in 12.5 per cent and in 300 breasts containing cancer, in 7 per cent. The number of cases in either group is insufficient to give reliable percentage figures by decades, but this is nevertheless shown in Table XVI.

TABLE XVI
INCIDENCE OF SCLEROSING ADENOSIS

Decade	Number of Noncancer Cases with Sclerosing Adenosis	Number of Cancer Cases, with Sclerosing Adenosis
20-30	5	0
30-40	4	2
40-50	16	9
50-60	0	3
60-70	0	6

The only impressions that can be gained from Table XVI are that sclerosing adenosis (in essence, the focal microscopic form) is most common in the decade 40-50, and that the lesion, as such, can endure in the breast far beyond the menopause.

Table XVII shows the lesions that occur together with sclerosing adenosis

TABLE XVII
LESIONS ACCOMPANYING SCLEROSING ADENOSIS

	26 Noncancer Cases with Sclerosing Adenosis	200 Noncancer Cases	20 Cancer Cases with Sclerosing Adenosis	300 Cancer Cases
1 Hyperplasia of duct epithelium	60%	39%	85%	57%
2 Duct papillomatosis	56%	29%	75%	36%
3 Intracystic papilloma	0%	2%	0%	1%
4 Blunt duct adenosis	60%	26%	60%	26%
5 Apocrine epithelium	52%	42%	70%	39%
6 Fibro adenoma	16%	19%	5%	6%
7 Tendency to fibro adenoma	4%	3%	5%	6%
8 Cysts	64%	53%	60%	27%
9 Stasis and distention of ducts	32%	36%	65%	42%
10 Duct metaplasia	44%	34%	75%	45%
11 Periductal mastitis	26%	22%	20%	14%
12 Fat necrosis	0%	2%	0%	1 3%
13 Lobule frequency				
Numerous	28%	13%	10%	10%
Average	52%	61%	45%	35%
Few	20%	26%	45%	55%
14 Periductal myoid atrophy	36%	27%	55%	42%

From the foregoing it is clear that other cystic and proliferative lesions of types previously mentioned, tend to occur along with sclerosing adenosis, and, moreover, they occur with greater than usual frequency. One proliferative lesion, fibro-adenoma, does not follow this trend nor has it done so in former analyses.

It does not seem possible to show a fundamental difference between cancerous and noncancerous breasts on the basis of sclerosing adenosis. That this lesion has little or no part to play in mammary carcinogenesis we now feel reasonably certain. We have never seen any crucial morphologic evidence in any case that a mammary carcinoma was arising on a basis of sclerosing adenosis. The very occasional case in which cancer and sclerosing adenosis merge in the same microscopic field has always shown more convincing evidence of origin from other sources or simultaneously in sclerosing adenosis and other sources, so that satisfactory traceability to sclerosing adenosis as a precancerous entity has been lacking and the coexistence attributed to chance. For years, conservative local surgery has been recommended in cases of sclerosing adenosis, and no incident yet has occurred to alter this point of view.

The etiology of this lesion is unknown. The microscopic appearance does not change with phases of the menstrual cycle. Menstrual histories of the patients reveal nothing characteristic. In one case the patient, age 24, presented a 1.5-cm lump in her breast that had been present and unchanged for six months. A 20 mg pellet of estradiol was implanted adjacent to the lump. During 12 weeks of observation the lump in her breast changed not at all in character. At the end of this period the pellet and the breast tumor with adjacent breast tissue were excised. At the time of removal

the pellet weighed 14 mg. The 1.5-cm mass was a fibro-adenoma, with focal areas of sclerosing adenosis. In the adjacent breast tissue were additional foci of sclerosing adenosis. All areas of sclerosing adenosis were similar in structure and in the phase of fibrous sclerosis. None of the usual features of the florid phase was seen. This case was of interest because of the apparent negative response of the sclerosing adenosis (and for that matter the surrounding breast tissue) to estradiol administration.

Highly florid focal sclerosing adenosis has been observed in the breast of one pregnant patient. However, comparison with florid lesions in breasts of nonpregnant individuals renders it impossible to state that the concomitant pregnancy increased the floridity of the lesion, since equal degrees of floridity occur quite apart from pregnancy. Every phase of the process has been seen in individuals who have never been pregnant, from which it is obvious that pregnancy is not a necessary initiating growth factor, and it is not a postlactational involutional phenomenon. Material studied to date has given no clue to what initiates the early or florid phase. It can be said that this pattern is much more common in the third and fourth decades, but on occasion unusually florid cases are seen in older women, an extreme example being in a patient age 62. The period during which a lesion may remain in a florid phase is also indeterminate but this character was seen in one tumor whose presence had been known for 12 years. In another florid case, the lump was first noted shortly after injections of unstated amounts of theelin. In still another case the lump was observed prior to theelin therapy, and after administration of 100,000 units, the symptoms of lump were said to have been partially relieved. In the section, however, the histology was anything but that of a lesion presumably "relieved," the florid characters being extremely prominent. These chance observations cannot, of course, answer questions on etiology, but they tend to emphasize the unpredictability of hormonal influences.

VII — PERIDUCTAL MASTITIS

The most common histologic feature of periductal mastitis is more or less inflammatory cell infiltrate about the mammary ducts, the predominant cells usually being lymphocytes. The appearance of inflammatory cells, however, is in nearly every case preceded by other changes, namely, stasis of amorphous acellular and cellular duct content, dilatation of the duct wall and varying degrees of atrophy of periductal myoid tissue. A common accompaniment of the process is flattening of the lining epithelium of the duct, usually slight, but in severe cases quite marked so that true squamous metaplasia results. Also, commonly observed are fat-laden phagocytes within the duct lumen, scattered or clustered among the lining epithelial cells and/or dispersed about the duct wall in varying numbers where they mingle with other cells, usually lymphocytes. If the lining epithelium and wall of a duct are eroded, it is not uncommon to find old or fresh blood in the lumen or adjacent periductal tissue, and this is responsible for some cases that

present clinically with bleeding nipple as the chief symptom. Every conceivable combination and degree of these changes are observed, but over-all the most constant finding is stasis of duct content. The cause of stasis is not apparent, but it is reasonably certain that anatomic obstruction to ducts is not essential. No doubt obstruction due to duct papillomas, pressure from cysts or tumors or senile atrophy with duct dilatation facilitate the process, but on close analysis these factors do not explain many of the cases. When these lesions seem concerned the periductal mastitis occurs distally. Such lesions seldom account for the most marked or extensive cases. In noncancerous papillomatosis of multiple small ducts, there is seldom associated periductal mastitis when the papillary lesions are early and small. A solitary macroscopic papilloma is far more apt to produce this lesion and the changes appear to depend on the production of stasis of duct content. Furthermore, in comedocarcinoma, where the ducts are lined by cancer cells and there is much central necrosis, somewhat analogous to ordinary duct stasis, periductal mastitis is common and apt to be severe.

One of the consequences of duct stasis is erosion of the epithelial lining. This commonly occurs with relatively little inflammatory reaction. When, however, the duct wall is weakened or penetrated the contents of the duct gain access to adjacent tissue and further changes ensue. If the duct is surrounded by dense fibrous tissue, the reaction produced is relatively mild and not extensive. But if the adjacent tissue is fatty, the outpouring of duct content is followed by a more severe and more complicated inflammatory reaction characterized by fat necrosis in which the break-down products of the fat tissue play an aggravating role. The end-result is the production of foreign body type of inflammation. Cholesterol, its esters, and fatty acids are found in these areas of inflammation and are easily identified as crystals or by special staining. The process can be extremely chronic, lasting for months and years. In fully developed form, a palpable mass may be produced and the breast present brawny induration. Secondary changes in the overlying skin sometimes occur, and it is readily understandable why on occasion a clinical diagnosis of cancer is made. This clinical condition has been described by Lee and Adair² under the designation "traumatic fat necrosis." It is notable, however, that many cases do not give a history of trauma, and when this is lacking the term "inflammatory necrosis" is a better one. Trauma is not an essential by any means to mammary fat necrosis, but one might postulate that trauma to a breast already the seat of stasis, distention and periductal mastitis augments the chances of that breast developing clinical fat necrosis. In summary, we regard periductal mastitis as representing only a part of a pathologic complex, usually preceded by duct stasis and impairment of the duct wall and followed in some instances by varying degrees of mammary fat necrosis. In this connection see Figures 22 through 25.

Periductal mastitis was found in 44, or 22 per cent, of the 200 non-cancerous breasts and in 44, or 15 per cent, of the 300 cancerous breasts

In the 44 noncancerous breasts with periductal mastitis, the average age of the patients was 41.7 years, while in the 44 cases of cancer with periductal mastitis the average age was 49.7. The occurrence by decades is shown in Table XVIII. On account of the morphologic relationship between

FIG 24

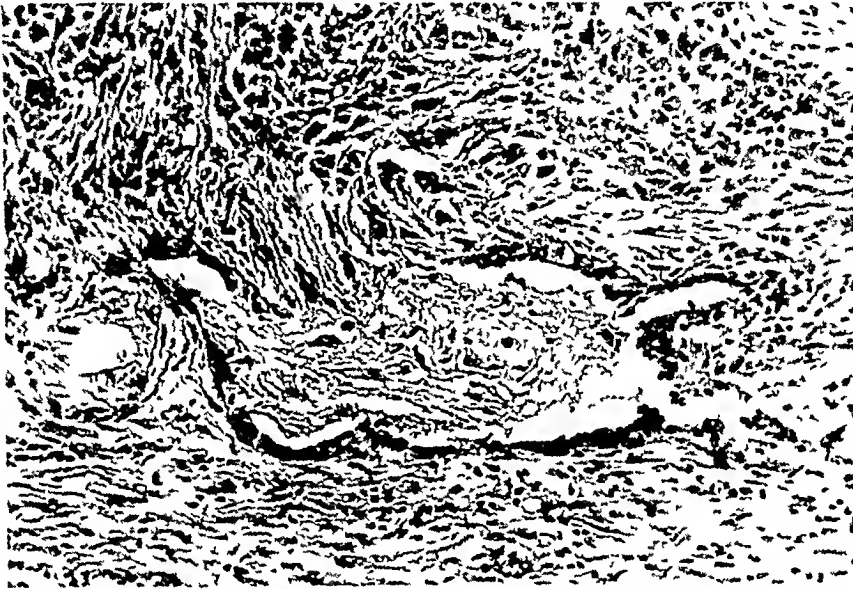


FIG 25

FIG 24 —Erosion of lining epithelium and duct wall. Escape of duct content and productive inflammatory response with foreign body characters.
FIG 25 —Sequela of leakage of duct content, fully developed inflammatory fat necrosis. Spindle shaped spaces mark former sites of crystalline material removed by solvent chemicals. Many foreign body giant cells.

periductal mastitis and combined stasis and distention of mammary ducts, figures for the latter are included.

The greater frequency of periductal mastitis in breasts without cancer is correlated in each age-group by a correspondingly greater frequency of stasis of duct content and duct dilatation. This statistical interrelationship would not be given so much weight if it were not for the fact that it is

TABLE XVIII

OCCURRENCE OF PERIDUCTAL MASTITIS, STASIS OF DUCT CONTENT AND DUCT DISTENTION

Decade	Noncancerous Cases		Cancer Cases	
	Periductal Mastitis	Combined Stasis and Distention	Periductal Mastitis	Combined Stasis and Distention
30-40	30%	40%	10%	28%
40-50	15%	48%	8%	30%
50-60	48%	70%	18%	48%

supported by morphologic relationship, the simultaneous occurrence of the lesions in the same microscopic or larger areas. Again, it is repeated as in former sections that statistical relations are insufficient for conclusions unless given meaning by concomitant anatomic correlation.

On close examination of periductal mastitis in both groups of cases, it is evident in each that most of these lesions are of slight extent, so that only 22 per cent of the noncancerous breasts with periductal mastitis and 18 per cent of the cancerous breasts with periductal mastitis show the lesion to marked degree. It is of interest that in the entire group of noncancerous cases with periductal mastitis, fat necrosis occurred six times and in every instance the periductal mastitis, stasis and distention were marked (Note that three of these cases of fat necrosis were from the additional cases added to the 50- to 60-year decade, and, hence, the total of six exceeds the number of cases of fat necrosis in the series of 200 noncancerous breasts). The same was noted in the cancer cases with periductal mastitis. In this group fat necrosis was found four times, always with marked degree of periductal mastitis, stasis and distention, and these cases constituted all examples of fat necrosis in the 300 cases of the cancer series.

Periductal mastitis in both the cancer and noncancer series, as previously mentioned, occurs chiefly with no demonstrable basis except stasis of duct content and dilatation. In the older age-groups this is apt to be rather diffuse (this seems related to the changes of senile atrophy) but may be predominantly focal. In younger women there is a greater tendency to focal distribution. In many cases the periductal mastitis is dependent upon local lesions such as duct papilloma and pressure from cyst or tumor. Thus we regard periductal mastitis in some cases as nonobstructive or "primary" and in some cases as obstructive or "secondary."

The cause for excessive stasis in the primary cases is not clear. The material apparently is composed of desquamative epithelial debris and it may be added to by products of secretion from or through lobular and duct epithelium. Perhaps these changes are due to excessive desquamation or secretion which exceeds the physiologic capacity of the mechanism normally disposing of duct content. Some of the marked cases do give a history of nipple discharge, but in most cases this does not occur. Periductal mastitis in minor form is no more apt to appear in breasts that have lactated than in those that have not, and multiple lactations do not play a part. We do not have enough data to state whether or not this is true of the most marked cases that present in a clinical form with segmental localization.

The presence of periductal mastitis in either cancerous or noncancerous breasts does not materially influence the occurrence of lesions other than those already mentioned as being fundamentally concerned in the process. When other lesions such as cysts and noncancerous proliferative processes are present, they never appear to begin as a result of periductal mastitis, stasis and distention of ducts or fat necrosis.

Any differences in cancerous and noncancerous breasts that show periductal mastitis are unimportant ones and depend almost exclusively on age distribution of cases. In none of the 300 cases of cancer could we trace the source of mammary carcinoma to periductal mastitis and its related lesions. The tracing of cancer to this source would, in our opinion, depend upon the demonstration of histologic transitions in the epithelium at such foci. Previously, it has been stated that the most common alteration in epithelial cells at such sites is metaplasia, usually of minor degree, and in some instances the production of true squamous characters. Another epithelial change fairly common at areas of periductal mastitis and stasis and distention is slight epithelial piling-up and loosening. This change is a minor one, usually seen in medium and larger ducts, and seems to be little more than trivial hyperplasia that desquamates rapidly. The stasis and distention as well as the periductal mastitis are usually slight in such areas, and it is almost invariable to find flattening and atrophy at sites of marked distention and periductal mastitis. It is not implied that an atrophic epithelium is unlikely to give rise to cancer. It can be said, however, that in the material studied here, no significant histologic atypism could be found in either atrophic or hyperplastic epithelium lining areas of stasis, distention and periductal mastitis. In the earliest mammary cancers seen by us in this and other material where the ducts were lined by typical cancer cells, periductal mastitis does not play the rôle of precursor.

VIII — THE MAMMARY LOBULES

The comparative examination of the character of the mammary lobules in cancerous *versus* noncancerous breasts has offered more difficulties than any other aspect of this morphologic analysis. That this has been the experience of other authors is indicated by the relative absence of detailed accounts of lobule abnormality. Perhaps these writers have felt the same major obstructing factor as we ourselves, namely, the problem posed by the question, what constitutes the normal lobule pattern of the human female breast and what changing aspects, if any, are imposed by the cyclic phases of menstruation? Insofar as we have been able to ascertain, there has been no morphologic survey of mammary lobules which has been based upon the examination of ideal material. Reports on breast tissue taken from autopsies have the disadvantage that they deal with specimens from chronic or acute diseases that may in themselves have been in part responsible for alterations in the lobule structure presented. Actually, the study of such breasts is a specific problem in itself, and should logically be prosecuted after a fundamental

normal has been established by study of "screened" material. The other source from which observations have been made is from surgical breasts, and these as a whole are *prima facie* abnormal organs. Even so, when one studies a large amount of such material and compares his findings with those of others, there seems no doubt that certain lobule patterns are more characteristic of one phase of the cycle than another. We have been able to study a limited amount of selected autopsy material and, in addition, over 300 surgical breasts from patients in whom menstrual dates were known. Our findings are in more or less agreement with the descriptions furnished by Rosenburg,³ Dieckmann,⁴ Polano,⁵ and Geschickter,⁶ and divergencies will not be elaborated here in histologic detail. Structural features that we consider indicative of various phases of the menstrual cycle are presented with explanatory notes in Figures 26 through 33.

After the study of material of the type mentioned above, much remains that is unsatisfactory. A vast majority of these breasts present a distinct variation in lobular structure, and it is the unusual gland that possesses even a moderately homogeneous picture. Certain of the lobule patterns when charted in relation to certain stages of the menstrual cycle will be found more commonly in the lutein phase, for example, and yet the chart will show these same types during the follicular phase and *vice versa*. Only a trend is shown. Added to this there are other types of lobules that show no relation at all to the periodicity of the ovarian cycle, and, moreover, they embrace a wide variety of structure quite different from that of those lobules which seem more characteristic of either the follicular or lutein phase. In our lack of understanding of the significance of these latter structural types, we pursued their study under the premise that they may represent abnormal lobule configurations. Almost at once, it became obvious that the lobules adjacent to such expanding lesions as fibro-adenoma and cyst or lobules at the edge of a cancer showed a series of changes not encountered when these lesions were absent. Chief among the changes seen were intralobular edema, irregular contour and size of lobules and their epithelial components, lack of uniform layering of acinar epithelium and intralobular round cell infiltrate. These changes apparently represented an early stage in what can be called secondary lobule alteration. The later stage of this process was accentuated by decrease or nearly complete loss of lobular epithelial components, replacement by dense round cell infiltrate and decrease or disappearance of lobular edema. Finally, lobular units were completely effaced and their former sites marked only by residual round cell foci with perhaps hyalinized acinar remnants. Of all these changes the marked intralobular edema seemed most common. Often these alterations involved lobules as much as 2 cm distant from the edge of a large, expanding lesion, they extended, as might be expected, a shorter distance when the expanding lesion was roughly 1 cm in diameter. In any breast containing many cysts and/or other lesions causing peripheral pressure, it can be easily seen that lobule homogeneity will in some measure be disrupted.

FIG 26

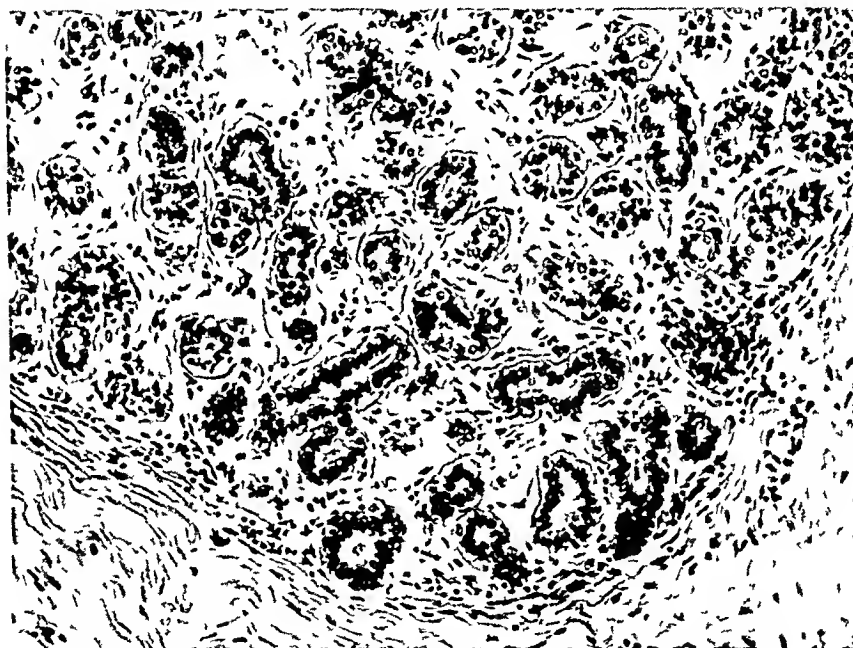


FIG 27

FIG 26 —Section taken on first day of menstruation. Acini are numerous and closely spaced. Lumina are open and contain secretion. Lining cells cuboidal to columnar, cytoplasm rather abundant and pale. Cell arrangement orderly. Full size of lobule not shown in this cross section. Stroma rather vascular and free from collagen. Occasional lymphocytes. Fully developed lutein phase of cycle. Appearance indistinguishable from many lobules seen in third month of pregnancy. Many lobules in this breast fail to show as marked luteinization.

FIG 27 —Section taken on fourth day after onset of menstruation. Early involutional changes. Acini continue to be numerous. Some lumina remain open, some narrowed, many closed. Residual secretion can be seen. Fewer columnar cells. Orderly cell arrangement persists in some acini but with contracture of acini and obliteration of lumina, cells are piling up in disordered fashion. Stroma showing early condensation and increased numbers of lymphocytes as well as decreased vascularity.

FIG 28

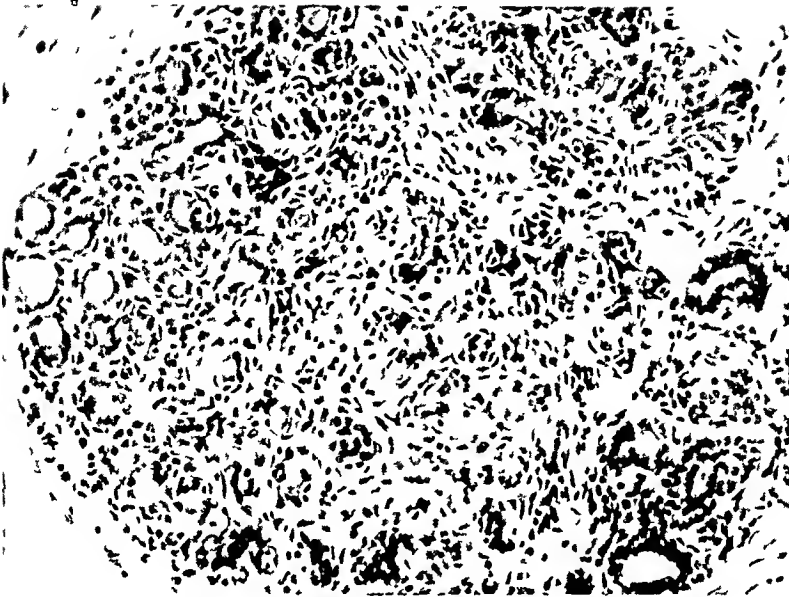


FIG 29

FIG 28—Section taken eight days after onset of menstruation. Further involutional changes. Process not entirely uniform but this is not unexpected. Central portion of lobule in advance of periphery. Some acini almost extinct. Increasing numbers of lymphocytes. (Compare with Figures 27 and 29).

FIG 29—From same section as Figure 28. Uniform and rather advanced involution. Acini still numerous but collapsed. Condensation of acinar cells. Reduction in size and nuclear pyknosis. Abundant lymphocytic infiltrate. Stroma somewhat less dense than ordinarily found eight days after onset of menses.

On further observation, secondary lobule alteration could be found in association with other breast lesions. Those lobules distal to an intraductal papilloma or comedocarcinoma were nearly always adversely affected. The general trend in these instances was toward atrophy following in the wake

FIG 30

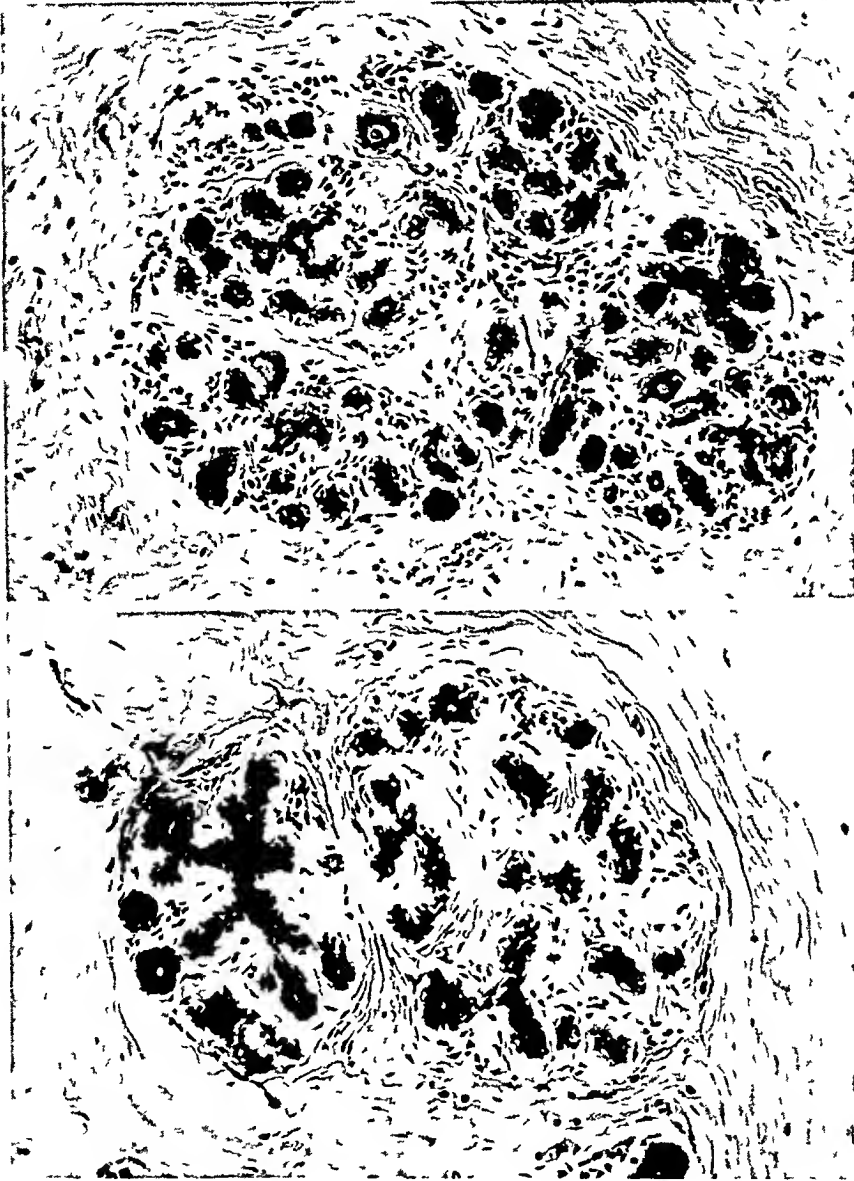


FIG 31

FIG 30—Section taken 12 days after onset of menstruation. Involution nearly complete. Acini less numerous, more widely spaced. Intervening stroma denser. Lymphocytes still present.

FIG 31—From same section as Figure 30. End point of physiologic involution. Few acini remain and these in collapsed state with hyaline connective tissue condensation about some. Remainder of stroma dense and practically free from lymphocytes.

of, and dependent upon the degree of the induced duct dilatation, stasis of duct content and periductal mastitis. In another section we have discussed the secondary formation of duct stasis, distention and periductal mastitis due to pressure from cyst, fibro-adenoma and cancer. Thus, any expanding

lesion of the breast may not only cause lobule alteration locally through pressure alone, but also at a greater distance by interference with adjacent ducts, the effects of which interference are detected in their corresponding lobular terminations. As expected, when the lesion complex of duct stasis,

FIG 32

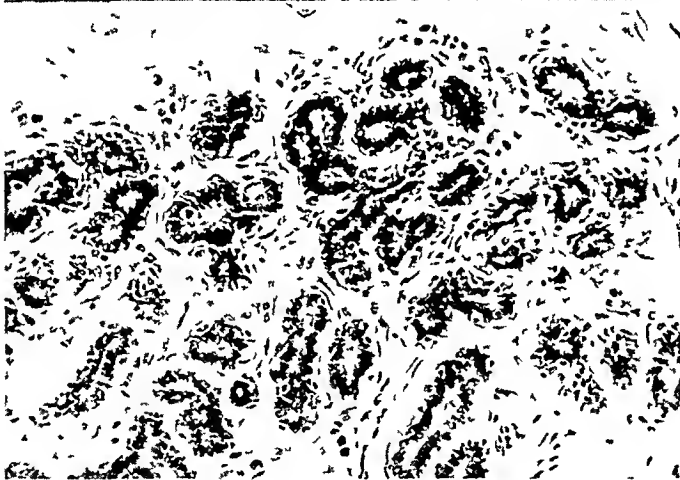


FIG 33

FIG 32—Section taken 15 days after onset of menstruation. Stage of reactivation. Note loosening of stroma as if in preparation for acinar hyperplasia. Connective tissue cells larger and less elongated. Occasional mitoses of these cells present but not visible at this magnification. Acinar lumina reestablished with lining cells assuming coherent arrangement. Nuclei remain dark.

FIG 33—Section taken 22 days after onset of menstruation. Characteristic corpus luteum effect. Multiplication of acini. Lumina present but not yet crowded with secretion. Lining cells larger and taller. Cytoplasm more abundant and nuclei relatively pale. Occasional mitoses can be seen with difficulty.

dilatation and periductal mastitis occurs in primary form, the lobules supplied by these ducts show the same changes as seen when the aforesaid lesion-complex of duct dilatation, stasis and periductal mastitis is of secondary type.

Those portions of breast tissue free from expanding lesions did not show the type of change referred to as secondary lobule alteration. In

sections of such tissue, however, it was common to see lobule patterns that did not fit the pictures associated with expected cyclic changes. The structural types seen were several in number, and as a general group may be referred to as primary lobule alteration. In some instances the lobules were uniform in appearance, and when such was the case, they tended to assume one of two forms. In the first of these the lobules were very few, they were quite small, the acini were scanty and reduced in size. The intralobular connective tissue was neither edematous nor dense, and periacinar hyaline was inconspicuous. Often there was considerable fat replacement of fibrous stroma. In short, this was a reproduction of an atrophic breast, and was what would be seen in the breast of a postmenopausal woman. On repeated occasions this sort of lobule pattern has been seen in women far short of the menopause. Extreme examples may be seen in the early twenties. Little or no difference was apparent regardless of the stage of the menstrual cycle during which the tissue was obtained. No accurate explanation can be made when such cases have normal menstrual histories, and such is usual in the cases seen thus far. The general impression is that such breast tissue may be refractory to hormonal influences. Verification of this hypothesis obviously depends upon demonstration of at least normal cyclic output of both the follicular and luteinizing hormones, since the mere existence of a normal menstrual cycle clinically perhaps tells us nothing of actual hormone patterns.

In the second type of primary lobule alteration where homogeneity of structure existed, the following was seen. The number of lobules was neither increased nor decreased. They were chiefly of average size. The intralobular connective tissue was abundant, loose and edematous. The epithelial components were very few in number but of large size, and the lining cells were often piled up in three to four layers and were rather apolar in arrangement. Seldom was periacinar hyaline a prominent feature. The most extreme examples of this type furnished at least a superficial resemblance to gynecomastia, particularly when the epithelial components of the lobule were very few in number. Again, this type of lobule structure has been encountered repeatedly without relation to any particular phase of the menstrual cycle. Any proposal that such a picture is the result of excess follicular hormone meets the embarrassment of one's inability to present the required proof by chemical assay.

The two types of primary lobule alteration just discussed are relatively infrequent, each being seen in about 5 per cent of surgical breasts. Far more common is a third form of primary lobule alteration in which the lobule pattern is unbalanced and irregular. A description of these changes is extremely difficult to put into words. The principal character is the heterogeneity which makes it utterly impossible to predict from sections at what stage of the menstrual cycle the tissue was obtained. Certain lobular groups suggest the lutein phase, while adjacent ones seem more characteristic of the follicular phase. Still others partake of neither of these phasic types. Sometimes the structure resembles the florid phase of lobular sclerosing adenosis, and in the

same section foci may occur that demonstrate the regressive phase of the same process. Still other lobules appear to be undergoing atrophy very much as in a senile breast, while others suggest an early phase of cyst formation as manifested by marked acinar dilatation. Intralobular epithelial hyperplasia of "nonphysiologic" kind is seen. This is commented on at a further point in this section. Added to these are "metaplastic" changes in which the acinar epithelium becomes flattened and almost epidermoid in character, or perhaps the acinar epithelium is seen in various easily traced stages of transformation to the so-called apocrine type. It is reasonable to assume that when such complex lobule arrangements are met, they represent multiple epochs of abnormal proliferation and involution, some of which may have occurred long before the specimen was secured.

To refer such changes as these to hormone imbalance is still problematical, and practically all of the evidence on human breasts comes from somewhat indirect sources. These sources include (1) the résumé of material which indicates certain types of lobules to be more characteristic of the follicular or lutein phase of the cycle, (2) the study of the human female breast under known preponderance of the corpus luteum hormone, that is, in pregnancy, and (3) the study of the male breast under conditions of known excess of female hormone, that is, in gynecomastia. Interesting observations could be made if one could secure breast tissue from patients who, on curettage, are shown to have glandular and cystic endometrial hyperplasia. The number of cases required to enable proper evaluation is discouraging. When one applies the structural evidence from sources that are available and makes comparisons with surgical breast preparations, it is difficult to deny a probable relationship to hormone imbalance. It seems possible that the implied imbalance need not require an excess of one or the other ovarian hormone, perhaps a subnormal amount of one or the other is sufficient. There is evidence that certain lobules are either more or less liable to hormone stimulation than are others. This is partially demonstrated by sections of the breast in various stages of pregnancy. Not every breast in the fifth to sixth week after the last menstruation shows the same degree of response, and as a matter of fact in some cases, one could not be sure of the existence of pregnancy from the sections, the appearance being so similar to that seen in a normal premenstrual breast. Even in the third trimester of pregnancy very small numbers of lobules may either appear almost totally unresponsive or much less well-developed than the vast majority of the lobular units. The rate of involution of individual lobules following pregnancy is also subject to demonstrable variation. Moreover, in examining a large number of breasts taken from one to ten years after the menopause, it is remarkable to note how capricious may be the rate of lobular atrophy.

The implications brought forward in the foregoing received some support when, late during the progress of this general study, we had the opportunity to examine breast material from another source. Through the aid of Doctor Sophie Spitz, and the courtesy of the Medical Examiner's Office of New

York City, specimens of both breasts and the endometrium were obtained. These were from cases of sudden death due to accident, homicide, or natural diseases, the latter being noninfectious in nature. There were two inter-related purposes in securing this material from cases of sudden death. First of these was to gain a more accurate insight into the frequency of the lesions of so-called chronic cystic mastitis in the breasts of the female population at large. The second was to ascertain the "average" appearance of the mammary lobules during the various phases of the menstrual cycle, as indicated by comparison with simultaneously taken sections of endometrium in cases without debilitating chronic disease. There were 27 such cases aggregating 54 breasts. Two of the cases were in the decade 10-20, three in the decade 20-30, thirteen in the decade 30-40, and nine in the decade 40-50. Not less than eight and an average of ten blocks were cut in each case, considerably more abundant sectioning than was done in the series of 500 cases reported here in detail. A thorough summary of this additional material will not be made here, but will be reported at a later date. The total number of cases is admittedly small, but there was so much structural contrast with the group of surgical breasts that some general comment seems warranted.

The lesions that have been presented in previous sections as constituting the complex of so-called chronic cystic mastitis were not absent in the material from cases of sudden death, but they were far less plentiful and by no means of as marked degree as seen in the cancerous or noncancerous surgical breasts. This was preeminently true in regard to gross lesions and equally true as regards microscopic lesions. The more plentiful sectioning of the material from instances of sudden death is, in our opinion, reinforcing, in that it affords less chance of failure to detect abnormalities.

The lobule status in the postmortem material was vastly different from that in the surgical material. In surgical breast material from premenopausal women, we find only about 10 per cent of cases that have enough homogeneity of lobule structure to justify a prediction of the phase of the menstrual cycle. After a certain degree of lobule imbalance is attained, any estimate is pure guesswork. Two of the 27 cases of sudden death showed advanced postmortem changes and were unsuitable for lobule or endometrial determinations. Three of these cases had atrophic endometria and were regarded as postmenopausal. Of the 22 remaining cases, two showed primary lobule alteration which made estimate of the stage of ovarian cycle unfeasible. Three of the cases showed the atrophic type of breast unsuitable for determining cyclic phases. There were 17 cases with uniform lobule structure which enabled one to estimate the phase of the menstrual cycle. In 16 of these 17 cases, the independent predictions of the cyclic phase by two observers proved correct, as controlled by the accompanying endometrial pattern. The prediction reported as a failure was correctly made by one observer. The sections of endometrium were, of course, not consulted until after the examination of the breast tissue. Excluding breasts and endometria showing too advanced postmortem change and those that were postmenopausal, there

were 22 cases. In 16 of these (72 per cent) it was possible to predict from the breast sections the phase of the menstrual cycle. This is in high contrast to the figure of 10 per cent obtainable by us in surgical breasts. In short, the homogeneity of the lobular structure of these breasts from cases of sudden death was directly contrary to the disordered lobular structure found in the surgical breasts. The far lesser incidence of the lesions of "chronic cystic mastitis" and the comparative absence of lobule alteration in the control (sudden death) breasts, combined with the high frequency of these lesions in the surgical breasts, suggests a close relationship between lobular alteration and the lesions we have presented in another section as constituting the complex of so-called chronic cystic mastitis. Perhaps certain forms of lobule alteration are an integral part of that complex.

In studying the occurrence of lobule alteration in the group of 300 cancerous and the 200 noncancerous breasts, observations were limited to the decades 30-40 and 40-50. Secondary lobule alteration was so common that no figures are given, and, moreover, it has already been stated that, anatomically, such changes seem secondary to pressure or duct stasis and associated lesions. The figures given in Table XIX concern only primary lobule alteration, as it has been described in the foregoing.

Table XIX indicates little except that in surgical material these lobule alterations are common, and that they are considerably more frequent in the later decade, as has been shown in preceding tabulations to be true of other lesions concerned in so-called chronic cystic mastitis.

TABLE XIX
INCIDENCE OF PRIMARY LOBULE ALTERATION

Decade	In Noncancerous Breasts Frequency in Per Cent	In Cancerous Breasts Frequency in Per Cent
30-40	36	34
40-50	52	48

The previous comments on lobule structure have referred to two general types of lobule alteration, primary and secondary, and were intended to direct attention to what may be considered abnormal lobule structure. It seems necessary here to discuss in some detail the problem of epithelial hyperplasia in lobules. Epithelial hyperplasia can be seen in lobules that show either primary or secondary alteration. A good deal of effort has been put forward in trying to establish what constitutes pathologic hyperplasia of lobular epithelium. The necessary criteria arrived at after prolonged consideration demand that the lobule under examination have an appearance dissimilar to that seen as a phasic pattern of the menstrual cycle or of pregnancy, the number of layers of lining epithelium must be greater than two (unless there is obviously a focal pile-up). If any part of a lobule shows such changes, epithelial hyperplasia is considered present. If such changes are limited to a single acinus, it is extremely uncommon in our experience. On many occasions, however, a relatively small part of a lobule may be affected. The occurrence of this sort of epithelial hyperplasia was

tabulated for the same material in which the incidence of lobule alteration was determined (Table XX)

TABLE XX
INCIDENCE OF INTRALOBULAR EPITHELIAL HYPERPLASIA

Decade	Noncancerous Breasts Frequency in Per Cent	Cancerous Breasts Frequency in Per Cent
30-40	14	16
40-50	22	34

FIG 34

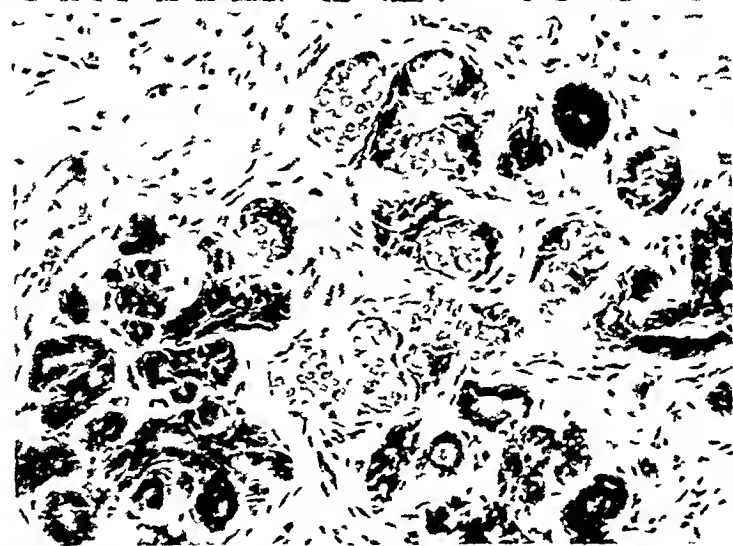
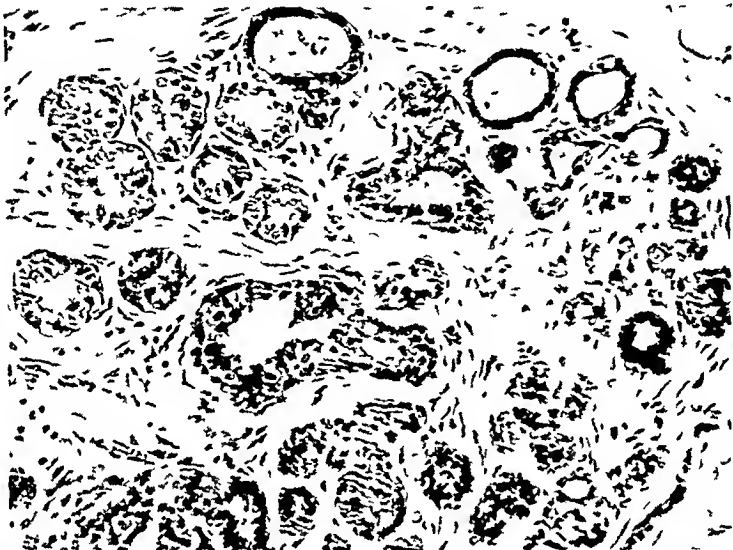


FIG 35

FIGS 34 and 35—Lobule patterns dissimilar to any seen as phasic variants of the ovarian cycle. Structural imbalance with multilayered lining cells in disorderly arrangement

The degree of epithelial hyperplasia in lobules, as one would anticipate, varied between broad limits from simple multiplication of lining layers to complete plugging of acinar lumina. A considerable experience is necessary before one's designations of epithelial hyperplasia in lobules are accurate and repeatable. Our plan was for each observer to make independent

recordings, compare results, review material where discrepancies occurred, and continue until each individual's observations were reproducible by the other. Several hundred breasts were studied in this manner before the above tabulations were made.

In a former paper⁷ the existence of and the histologic features of lobular

FIG 36

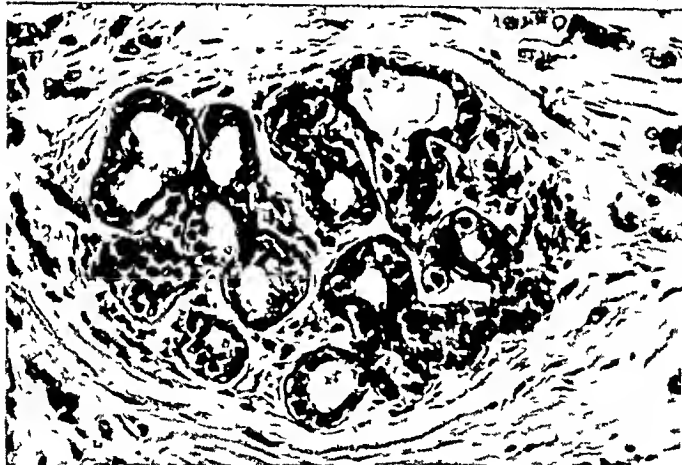
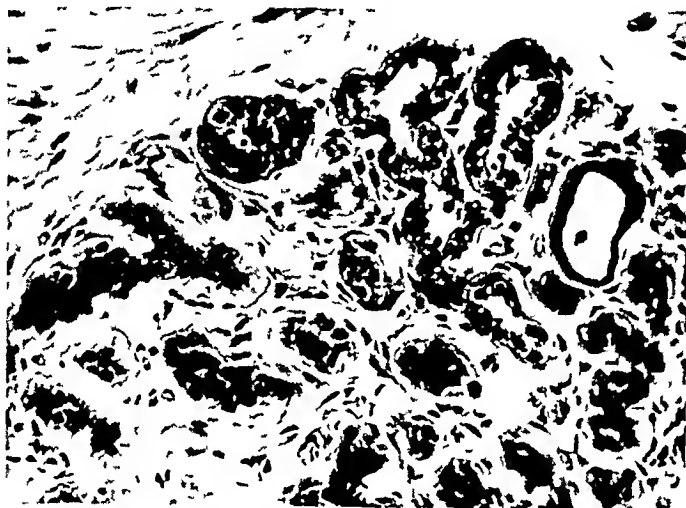


FIG 37

FIG 36—Lobular alteration, with pathologic hyperplasia of epithelium.

FIG 37—Appearance superficially suggesting corpus luteum phase of menstrual cycle, but there is stratification of lining cells, lack of coherent grouping and difference in cell size and staining properties. Moreover, patient beyond the menopause.

mammary carcinoma *in situ* were discussed. In addition, a brief description of the infiltrating phase of this type of mammary carcinoma was given. At that time no effort was made to depict histologic levels of lobular epithelial change that fell short of the fully developed *in situ* lesion. It was felt that such changes must exist, but we were not sure of their identity. The large mass of material examined in the past few years has made us much more confident of the earlier transitions to lobular mammary carcinoma *in situ*.

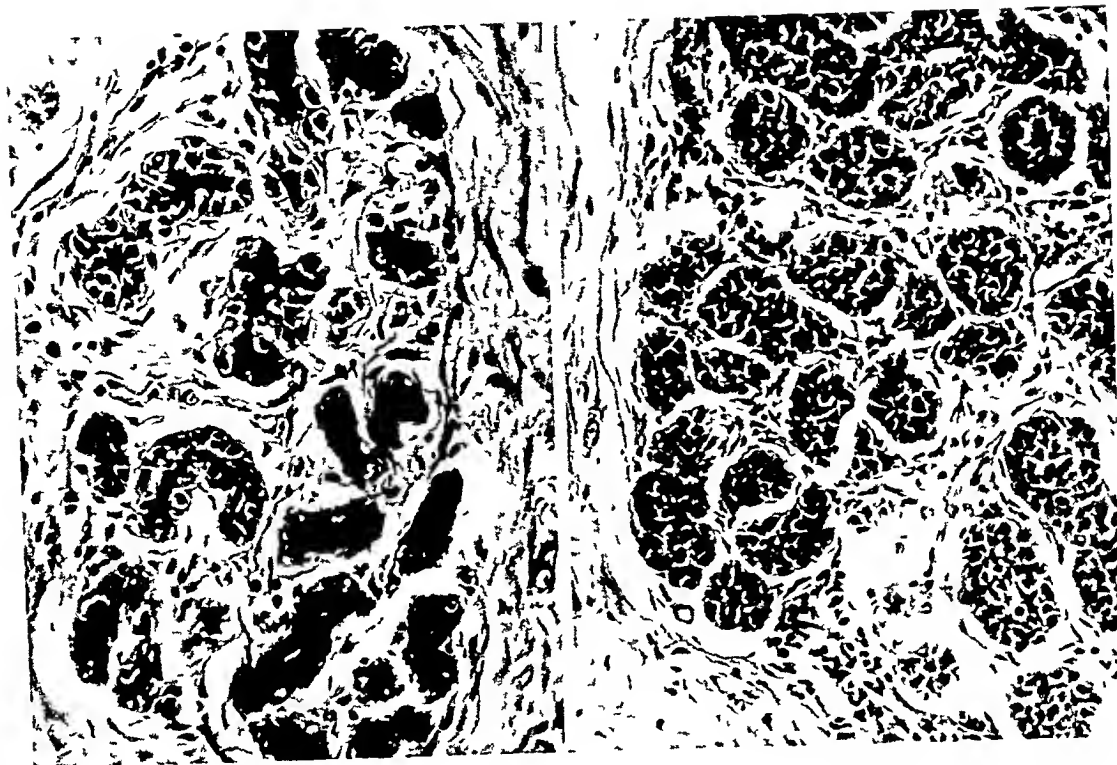


FIG 41

FIG 40—Another early phase of lobular carcinoma *in situ*. Note partial involvement.
FIG 41—Fully developed lobular carcinoma *in situ*. Acinar outlines still distinctly maintained.

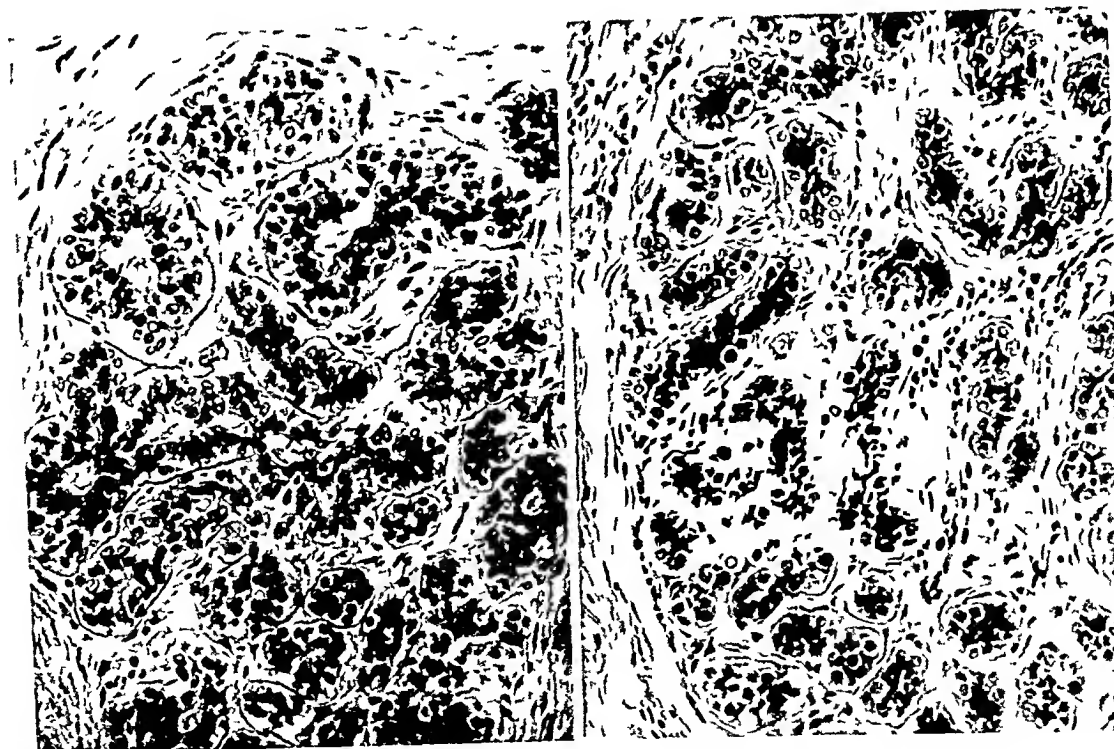


FIG 39

FIG 38—More advanced stage in hyperplasia of lobular epithelium. Structure distinctly atypical with deep stratification or plugging of lumina. Lack of polarity with pleomorphism and variable staining qualities. Mitoses seen, but not at this magnification. (Compare with Figures 37 and 39).
FIG 39—Interpreted as an early stage of lobular carcinoma *in situ*.

To write a word-formula for the identification of these subtle alterations is beyond our powers. The photomicrographs shown in Figures 34 through 43 illustrate variable degrees of lobule alteration with progression to lobular mammary carcinoma both *in situ* and in an early infiltrative phase. These may suffice in part, but they cannot substitute for actual retinal images. Once the actual histologic pictures are grasped, they appear to one as highly

FIG 42

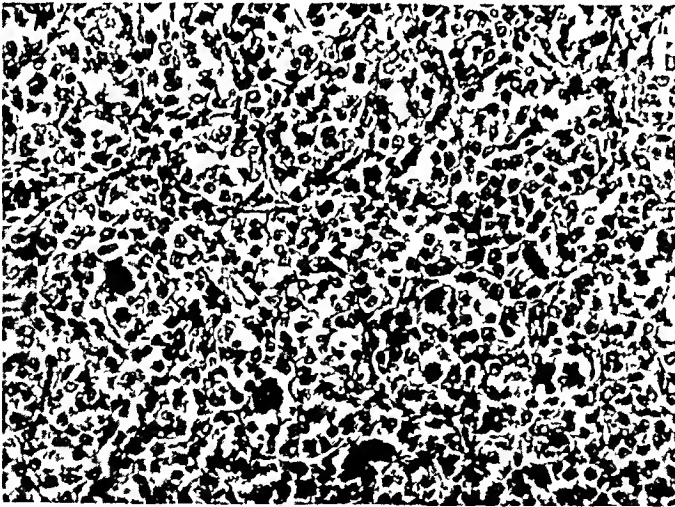
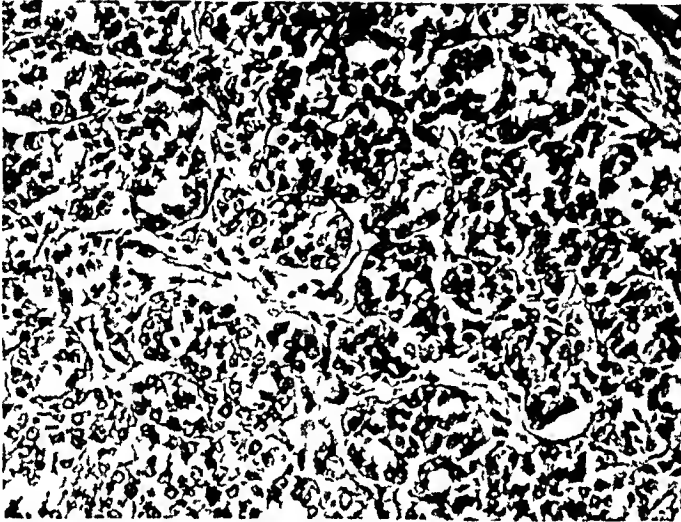


FIG 43

FIG 42—Further progression of lobular carcinoma *in situ*. Integrity of individual acini difficult to detect at all points.
FIG 43—Merging of acini and start of infiltrative stage.

characteristic and separable from other more common pictures of hyperplasia in lobules.

We regard certain atypical hyperplasias as transitional stages in the development of *in situ* lobule cancer. In a preceding section, it has been shown that one of the chief differences between cancerous and noncancerous breasts was the far greater likelihood that the cancerous breasts would show

duct papillomatosis of atypical structure. For this reason it seemed necessary to investigate atypical hyperplasia in lobules for the same relationship. In the material used for other lobule studies, there were 100 noncancerous breasts equally divided between the decades between 30 and 50 years. Not a single case was found in which there was atypical hyperplasia in lobules. This absolute absence is one of chance, since in about 500 noncancerous breasts seen yearly at Memorial Hospital, this atypical form of hyperplasia is seen about half a dozen times. We do not refer here to true lobular carcinoma *in situ* but the less advanced lobular alteration.

In 32 cancer cases between the ages of 30-40 and 50 cancer cases between the ages 40-50 there were six which showed the atypical form of intralobular epithelial hyperplasia. In four of these six cases, the cancers had the infiltration pattern so characteristic of cancers of lobule origin. In this group of 82 cancers, some form of epithelial hyperplasia in lobules was seen in 22 cases. In those 22 cases there were nine lobular mammary carcinomas, an incidence of 40 per cent, while the over-all incidence of lobular carcinoma is only about 5 per cent. These findings lead us to believe that the epithelial hyperplasias discussed do have a positive relationship in the development of mammary carcinoma of lobule origin.

In comparing the lobular structure of cancerous and noncancerous breasts, abnormal types are common in each group. One fundamental difference is found. This is the much more pronounced tendency for the lobules of breasts with cancer to show intralobular epithelial hyperplasia of atypical sort.

(To be continued)

CURLING'S ULCER IN EXPERIMENTAL BURNS*

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ULCERATION OF THE DUODENUM associated with burns has occurred in 12 per cent of animals utilized in an experimental study of burns projected by the National Research Council, and carried out at the Henry Ford Hospital. The material on which this presentation is based consists of 34 instances where ulceration of the duodenum was found associated with the experimental burn. An analysis of this material seems worth while in view of the fact that (1) Harkins¹ found only 98 Curling's ulcers in 680 burn cases reported up to 1938, of which 26, or 3.8 per cent, were confirmed by autopsy, (2) Curling's ulcers, that is ulcers of the duodenum subject to perforation and hemorrhage, have not been consistently produced experimentally, (3) this series shows a strikingly higher incidence in animals treated with bland dressings, such as sterile vaseline, in contrast to those treated with tannic acid, ferric chloride, silver nitrate and other tanning agents, (4) lethal complications of these ulcers have occurred in nine instances, hemorrhage four times, and perforation with peritonitis five times, and (5) the pathogenesis and the definite relation to burns have not been established.

Pack,² in 1926, and Harkins,¹ in 1938, made comprehensive reviews of duodenal ulcers associated with burns, first collected and described in detail by Curling³ in 1842. Cooper,⁴ in 1839, and Long,⁵ in 1840, had reported individual cases previous to Curling's consideration of the subject.

Although the 3.8 per cent incidence of autopsied cases quoted from Harkins represents a large series, it should be kept in mind that the percentage varies in this group from zero to 36.5, and that in the larger series the incidence is relatively low—Erichsen,⁶ 1895, 94 cases, or 2.1 per cent, Stewart,⁷ 1923, 115 cases, or 1.7 per cent, Harris,⁸ 1929, 138 cases, or 0.7 per cent, and Riehl,⁹ 1930, 152 cases, or 3.3 per cent.

As to pathogenesis, Pack lists ten theories and Harkins 26. Only those hypotheses supported by some objective evidence, clinical or experimental, will be enumerated here.

1. Hyperacidity of gastric secretion—Neches and Olson,¹⁰ 1941, found a great increase in gastric motility, and in a number of animals a considerable increase in the volume and acidity of the gastric secretion. Wilson,¹¹ 1935, failed to show hyperacidity in patients.

2. Action of burn toxin—Harris,⁸ 1929, ascribes Curling's ulcer seen in a three and one-half-year-old child to "protein metabolites" formed by digestion in the burned area. He believes this toxin produces focal necrosis and hemor-

*The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Henry Ford Hospital.

change in the duodenal mucosa and that these are, in turn, transformed into ulcers by the pancreatic juice Kapsinow,¹² 1934, pointed out from his work on rabbits that blood concentration results in stasis with rupture of the capillaries underlying the duodenal mucosa with tissue anoxia, necrosis and ulceration

3 Blalock,¹³ 1931, demonstrated low blood volume in burned animals, and Brooks and Blalock,¹⁴ 1934, showed necrosis, congestion and hemorrhage in both the duodenum and adrenals after producing a low blood volume by slow bleeding More recently, Freeman, *et al*,¹⁵ 1942, and Wiggers,¹⁶ have shown congestion of the duodenum in hematogenic shock

4 Perry and Shaw,¹⁷ 1894, pointed out that in septic conditions petechiae occur in serous and mucous membranes throughout the alimentary tract, and expressed the opinion that these petechiae served as the initial lesion from which duodenal ulcers in both septic processes and in burns develop Hertz and Digby,¹⁸ 1913, and Stewart,⁷ 1923, supported the view of Perry and Shaw, pointing out that the incidence of Curling's ulcers was reduced by antiseptic and aseptic surgical treatment

EXPERIMENTAL PROCEDURES

The material forming the basis for this presentation consists of 32 instances of gastric and duodenal ulceration occurring in the course of 80 experiments in which third degree burns were produced over 50 to 60 per cent of the body surface, while the animals were under morphine and ether, or morphine and chloroform anesthesia Following the procedure, liberal use of morphine and complete dressings kept the animals comfortable, as evidenced by the fact that they were active and retained a good food intake until the terminal stages

In the first group of seven experiments involving large burns, two were dressed with sterile vaseline, four with tannic acid and one with sulfadiazine and lanolin One vaselined animal survived only four days but the second lived eight days, and showed multiple small, punched-out duodenal ulcers The other members of the group lasted from eight to 13 days, but failed to show ulceration

Following this observation, a series of four animals, Nos 3095, 3096, 3097 and 3098, were burned and dressed with sterile vaseline Survival time was 10, 10, 13 and 10 days respectively Numbers 3095 and 3097 had large, punched-out duodenal ulcers, measuring 2 x 1 cm and extending down to the serosa Number 3096 had multiple small ulcers, 1 to 2 Mm in diameter in the prepyloric region of the stomach, while No 3098 had a superficial mucosal ulcer, 1 x 1 cm, in the duodenum All of this series showed extensive infection of the wound, *B coli*, *B proteus*, *B lactis aerogenes*, *Streptococcus hemolyticus* and *nonhemolyticus*, *Staphylococcus albus* and *Cl bifementans* being isolated Number 3098 showed *Streptococcus hemolyticus* in blood cultures Terminally, the blood plasma proteins were 5.4 Gm, N P N 75 mg, CO₂ 17.7 vol per cent, calcium 10.1 mg, and icterus index 15

Out of the first seven animals burned and dressed with sterile vaseline the five living eight days or more showed infection of the wound and gastric or duodenal ulceration

In the second group of experiments sterile vaseline, scarlet ointment and lanolin were used ten times, resulting in ulceration of the duodenum three times and of the stomach once

FIG 1

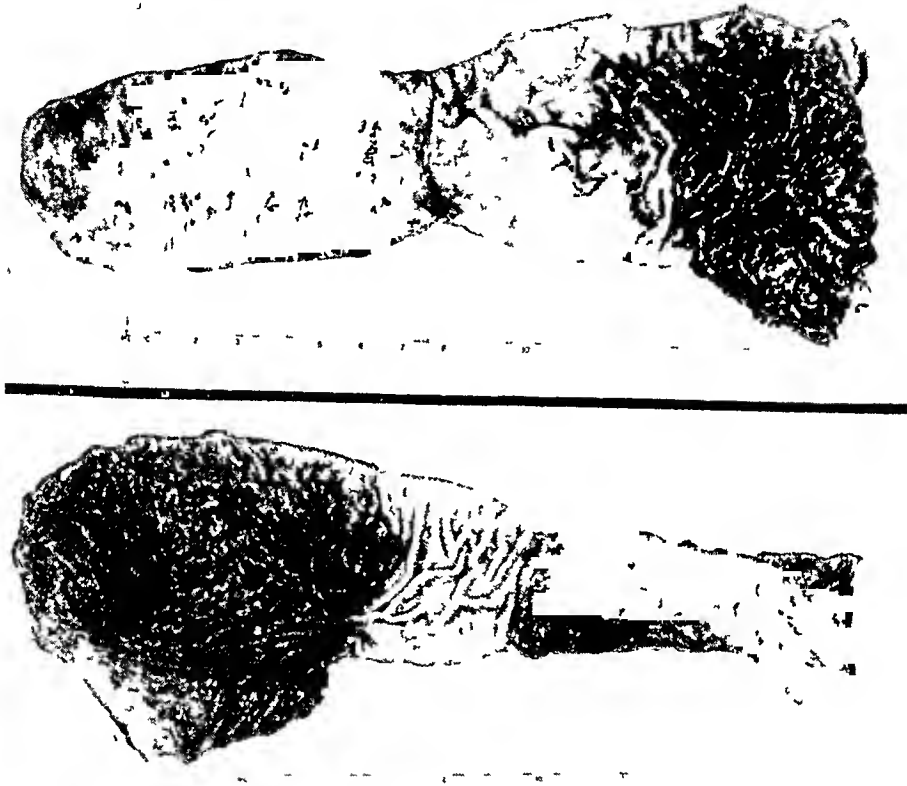


FIG 2

FIG 1—Experiment No 3180—Burned 60 per cent of body surface with steam, under chloroform anesthesia Dry dressing with 7.5 per cent tannic acid Survival time four days Autopsy Liver large, congested, kidneys large, congested, duodenum and fundus of stomach showed marked edema and congestion

FIG 2—Experiment No 3157—Received 150 cc neutral tannic acid subcutaneously, while under ether and morphine anesthesia Deeply jaundiced by third day Hb 50, blood sugar 76, hematocrit 67, survival time three days Autopsy Hemorrhagic pneumonia, bilateral, marked congestion of fundus of stomach and duodenum

Combining the two groups outlined above, there are a total of 17 burns dressed with vaseline and similar dressings, with 11 resulting ulcerations, or an ulcer incidence of 64.7 per cent It may be significant that two of this group failing to show ulceration were dressed with scarlet ointment and sulfadiazine-lanolin, respectively Both of these had minimal infection as compared with the rest of the group

In the second series there were 33 experiments This differed from the first group in that all the dressings were of sterile vaseline These dressings were not changed, and every effort was made to increase the survival time by special feeding and intravenous fluids The average survival time was

only slightly prolonged, however, and five animals were lost during the first five days. Of these only one, No. 3220, showed duodenal ulceration. Ulceration was found 21 times, or in 63.6 per cent. Two animals, Nos. 3255 and 3259, had perforating ulcers, with peritonitis, and one died from hemorrhage (No. 3220). In one group of three, surviving 9, 10 and 10 days, respectively, the incidence of ulcer was 100 per cent, and in nine successive experiments only one failed to show ulceration. This failure was possibly due to the fact that we succeeded in keeping the animal alive but five days.

In reviewing the second series of experiments, the loss of appetite, loss of weight, necrosis and infection of the wound, the marked loss of plasma into the dressings, the high nonprotein nitrogen of the blood, low CO_2

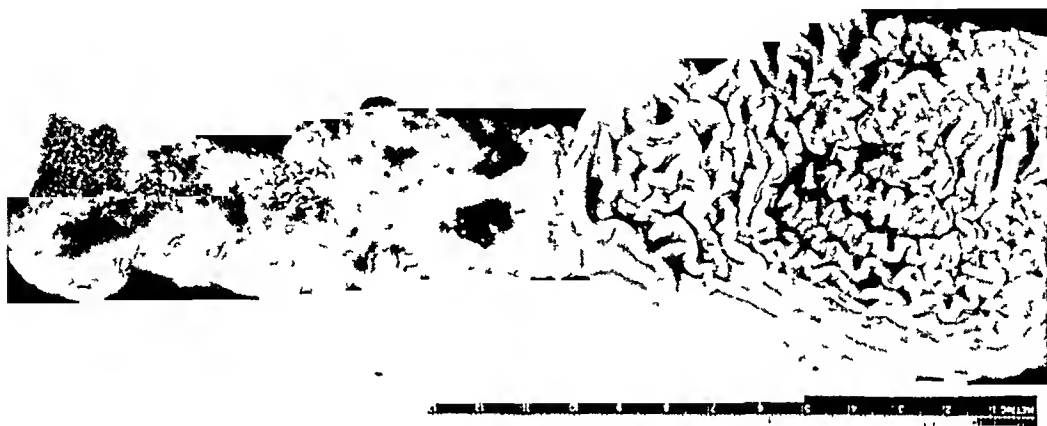


FIG. 3.—Experiment No. 3130.—Burned 60 per cent body surface, under chloroform and morphine. Dressed with sterile vaseline and gauze. Survival time six days. Autopsy. Two large mucosal ulcers of duodenum, associated with swelling and edema of the duodenal wall.

combining power of the blood, and the frequent coma with convulsions are clinical observations to be noted. At autopsy, the high incidence of acute ulceration of the duodenum, with no other equally consistent pathologic finding except the congestion and parenchymatous degeneration of the liver and kidneys is striking.

DISCUSSION—In the first series there were 47 third degree burns involving from 50 to 60 per cent of the body surface, with 13 showing ulceration of the duodenum or stomach. Thirty of these burns were dressed with tanning agents, such as tannic acid, ferric chloride, and silver nitrate. In this group ulceration occurred only twice, or in 6.6 per cent, and then only in those having wet dressings. Of the 17 dressed with vaseline, lanolin and scarlet ointment 11, or 64.7 per cent, showed ulceration. In the second series of 33 animals with burns of similar type all were dressed with sterile vaseline and 21, or 63.6 per cent, showed duodenal ulceration.

The gross examination of the duodenal ulcers reveals erosions from the most superficial mucosal lesions to penetrating incisive lesions with hemorrhage or perforating punched-out lesions, with peritonitis. The inflammatory infiltration is mild or absent in most cases, with acute exudate reaction found in only one section. A few healed ulcer craters and large scarred areas of the duodenal wall were observed.

Although duodenal ulcers were encountered in animals living from six to 23 days, the marked edema and congestion of the duodenum, and less frequently of the stomach, in one to three days after the burn, has to be given consideration as a basic or underlying lesion, especially since it has

FIG 4

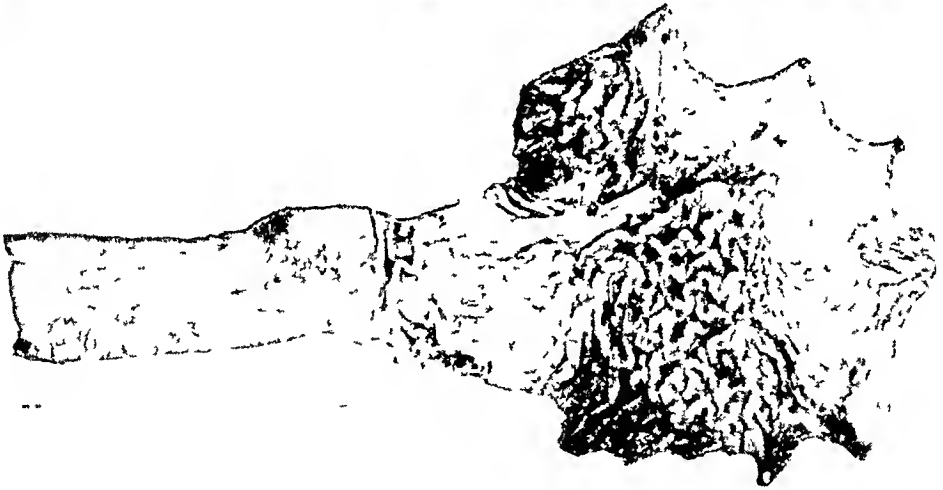


FIG 5

FIG 4—Experiment No 3142—Burned 60 per cent body surface under morphine and chloroform anesthesia. Wet dressing with 7.5 per cent tannic acid jelly. Remained in good condition for eight days, then began to pass blood per rectum. Died on ninth day. Autopsy. Wound not tanned but shows extensive necrosis and severe infection. Intestine filled with fresh blood coming from two ulcer craters in duodenum. One crater has large clot adherent. Vaseline and gauze. Showed extensive necrosis and infection. Survival nine days. Autopsy. Marked congestion of stomach and duodenum with multiple small ulcers.

been demonstrated in other types of experimental shock. Indeed, this lesion seems another manifestation of the pathology of shock comparable to the early engorgement and congestion in the liver, which probably initiates the degenerative or necrotic changes in that organ.

A comparison of the gastric contents, both fasting and after 150 cc of 5 per cent alcohol, of the normal and that of the burn dog at various stages shows that both the free hydrochloric acid and the total acid are reduced sharply rather than increased. This is in agreement with Wilson's¹¹ findings in the human, and not in accord with Necheles and Olson¹⁰. The other significant finding in the gastric contents was the blood, frequently seen as shreds and clots, and giving strongly positive chemical tests. This, coupled with the appearance found at autopsy, emphasizes the damage to the mucosa, preceding ulceration or in the absence of the same (Table I).

FIG 6

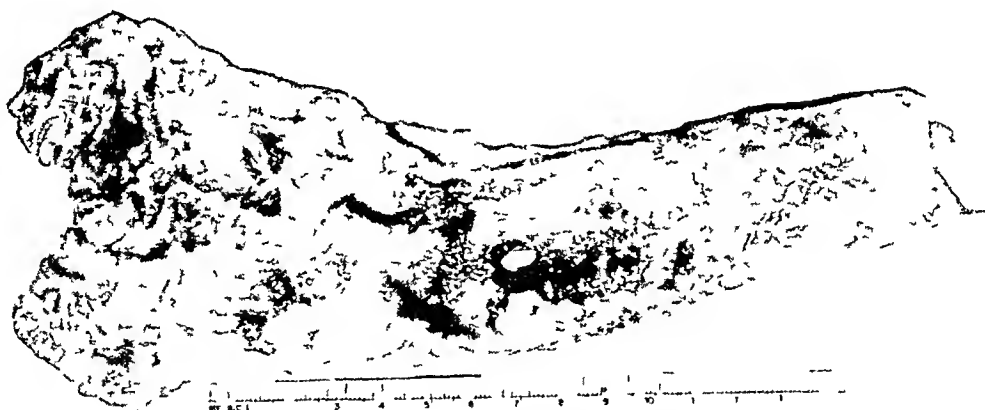
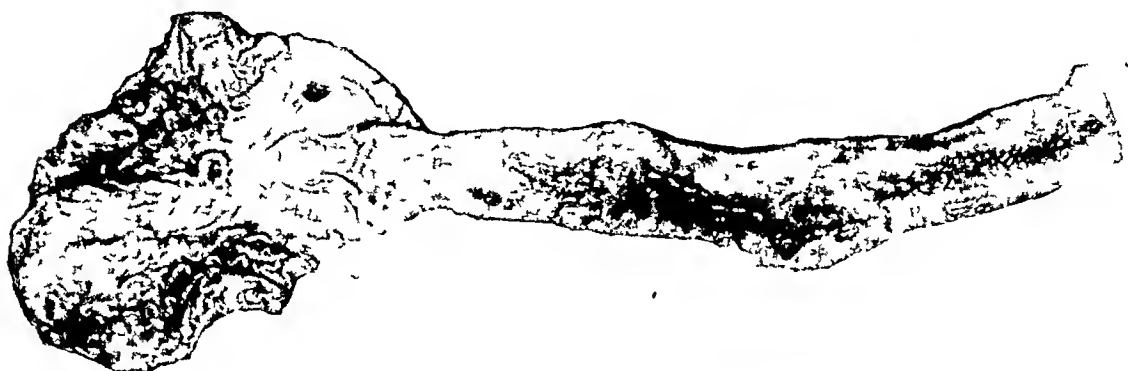


FIG 7

FIG 6—Experiment No 3262 Burned 60 per cent body surface Vaseline and gauze dressing. Animal ate well for first ten days. Gastric analysis on eleventh day: Free HCl 6, total acids 58, occult blood +++ Showed extensive necrosis and infection. Survival 12 days. Autopsy: Stomach showed single ulcer, 1 cm in diameter, pyloric region, duodenum—multiple smaller ulcers.

FIG 7—Experiment No 3255—Burned 60 per cent body surface. Dressed with sterile vaseline and gauze. Showed extensive necrosis and infection but ate well for first eight days. Survival time ten days. Autopsy: Abdomen distended with generalized peritonitis. On opening the duodenum there is a perforating ulcer, 1 cm in diameter, with small erosions nearby.

Hyperacidity as explanation of Curling's ulcers has no support from our data, but normal acidity may be sufficient to cause ulceration in the edematous, congested mucosa of these burn animals. Further, it is quite possible that the usual alkalinity of the duodenal contents is reduced by mucosal damage and the developing general acidosis.

The liver showed extensive parenchymatous degeneration, especially at

the center of the lobule, but not the characteristic central necrosis except in those cases treated with tanning agents

The kidneys were large and congested, with infarcts and cortical abscesses in about 5 per cent. Acute parenchymatous degeneration was regularly found.

The lungs usually showed edema and congestion with frequent lobular consolidation in the dependent portions.

TABLE I
GASTRIC ANALYSES

Dog No	Specimen	Free HCl	HCl Def	Total Acids	Guaric
Normal dog	Fasting	24	0	90	Neg
	15 mins	10	0	25	Neg
	30 mins	2	0	20	Neg
	45 mins	2	0	18	Neg
	60 mins	0	10	24	Neg
Normal dog	15 mins	0	6	10	Neg
	30 mins	0	4	8	Neg
	45 mins	2	0	12	Neg
	60 mins	8	0	20	Neg
3263 (6th day)	Fasting	2	0	12	++++
	15 mins	4	0	6	Neg
	30 mins	4	0	8	Neg
	45 mins	14	0	22	++
	60 mins	22	0	30	++++
	75 mins	8	0	22	++++
3265 (6th day)	Fasting	10	0	12	++++
	15 mins	2	0	10	Neg
	30 mins	0	4	2	Neg
	45 mins	0	2	12	++++
3265 (8th day)	Fasting	2	0	8	++++
	15 mins	2	0	10	++++
	30 mins	0	4	12	++++
	45 mins	0	2	4	++++
	60 mins	0	4	14	++++

Careful gross and microscopic examination of the brain was made in those animals particularly which showed coma and convulsions. Grossly, there was marked engorgement of the cerebral vessels but actual hemorrhage and encephalomalacia could not be made out. Microscopically, the hypothalamus was given special attention because of the relation of lesions of this area to ulceration of the intestinal tract, as pointed out by Cushing. Pericellular and perivascular edema was striking, with cuff hemorrhages about the vessels in a few instances. Small areas of devastation necrosis in the hypothalamus were present in one animal.

The 63 per cent incidence of Curling's ulcers in the two series of animals burned and dressed with vaseline and other bland applications, as contrasted with the 6 per cent incidence in the group burned in a similar manner and dressed with tannic acid or other tanning agents, indicates that an analysis of the two groups may suggest etiologic factors. The animal whose wound is dry-tanned loses very little plasma from the body, although the area



FIG 9

FIG 8—Experiment No 3259—Burned 60 per cent body surface. Dressed with sterile vaseline and gauze. Extensive necrosis and infection of wound but appetite well maintained for first nine days. Survival time 11 days. Autopsy—Much free fluid in abdominal cavity and a perforating ulcer in the duodenum, 1.5 cm in diameter. There are several smaller erosions in both the stomach and the duodenum.

FIG 9—Experiment No 3097—Burned 60 per cent body surface, under morphine and chloroform anesthesia. Dressed with sterile vaseline and gauze. Remains comfortable, eating and drinking fairly well. Cultures from wound on fifth day show both hemolytic and nonhemolytic *Streptococci*, *Staph albus* and eight other nonpathogenic bacteria. On the sixth day plasma proteins 515 mg per cent, hematocrit 45. Survival time nine days. Autopsy—Two large perforating duodenal ulcers.

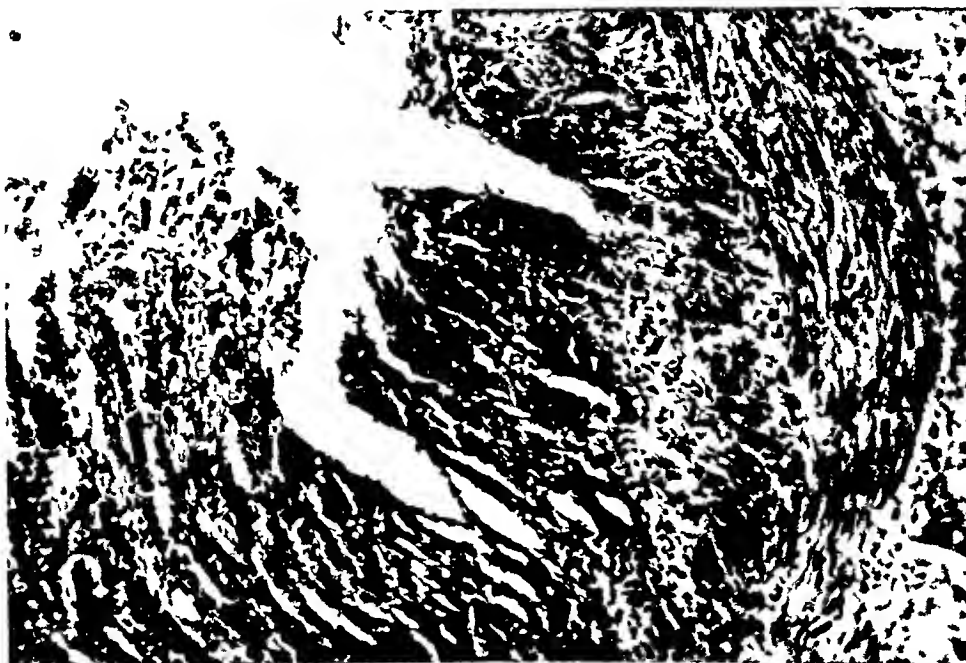


FIG 10—Dog No 3249—Photomicrograph showing small punched out ulcer extending through mucosa and submucosa. No evidence of inflammatory reaction (Low power).

beneath is always very edematous. The infection in such a wound is usually slight or absent up until the fourth or fifth day, when marginal separation of the eschar begins. The animal is comfortable and eats well after the first 36-48 hours. Marked acidosis rarely develops and, barring liver necrosis, a good recovery, with eventual healing of the skin defect, is accomplished.

Animals treated by moist dressings with tanning agents have a course more like the animals dressed with bland preparations except that necrosis and infection is somewhat reduced. With the bland dressings the injured



FIG 11—Dog No 3208—Photomicrograph showing smallest mucosal erosion, with no inflammatory reaction (Low power)

tissue rapidly begins to undergo autolysis. This, coupled with great and continued loss of plasma into the dressings, favors extensive infection with the various types of organisms listed. The appetite is reduced, so that despite careful feeding there is marked weight loss, acidosis, septicemia, coma and convulsions are frequent. Loss of plasma, rapid autolysis of injured tissue with infection and acidosis are the factors found in this group which may logically be cited as the variables responsible for duodenal ulceration and death.

SUMMARY

1 Fifty animals had third degree burns of 50 to 60 per cent of the body surface produced and dressed with vaseline or similar preparations. Curling's ulcer was a complication in 32, or 63.3 per cent.

2 Thirty animals had third degree burns of 50 to 60 per cent of the body surface produced, and were dressed with tannic acid or other tanning agents. Curling's ulcer was a complication in two, or 6.6 per cent, and in these the dressing was of the wet type.

3 Loss of plasma, autolysis with infection, and acidosis occurring in the first group, with 57 per cent higher incidence of Curling's ulcers over the second group, suggest themselves as etiologic factors.



FIG 12—Dog No 3099—Photomicrograph showing thickened, infiltrated duodenal wall, with deep ulcer (Low power)



FIG 13—Dog No 3256—Photomicrograph showing shallow ulcer extending to submucosa (Low power)

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TRANSTHORACIC ESOPHAGOGASTROSTOMY FOR CARCINOMA OF THE MIDDLE THIRD OF THE ESOPHAGUS

REPORT OF A SUCCESSFUL RESECTION

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AT THE PRESENT TIME transthoracic resection for carcinoma of the lower third of the esophagus with esophagogastrostomy has become a well-standardized procedure which can be performed with considerable success

Progress in the surgical treatment for carcinoma of the middle third of the esophagus has not kept pace with that of the lower third or with other thoracic tumors Until recently all of the carcinomas of the middle third were resected by the method used and developed by Torek¹ Although this procedure fulfills the principles of good cancer surgery it is not entirely satisfactory, in that esophagogastric continuity is not reestablished

The cervical esophagostomy may be connected to the abdominal esophagostomy or gastrostomy by means of an anterior thoracic esophagoplasty or, if such is unsuccessful a rubber tube The rubber tube connection is an unending source of complaints The tube frequently becomes dislodged or plugged and is almost constantly leaking Many ingenious methods have been proposed for anterior thoracic esophagoplasty utilizing skin tubes (Bücher) stomach (Kirschner) gastric tube (Beck, Jianu), jejunum (Roux, Herzen), colon (Vulliet-Kelling), and a combination of jejunum and skin tube (Lexer, Wullstein) Most of these operations require multiple operative procedures and are quite difficult to perform Yudin² has recently reported the construction of an artificial esophagus in 80 cases of stricture of the esophagus In six of these he used Bücher's cutaneous tube method, 16 had a direct anastomosis performed between the pharynx and a jejunal transplant, and 58 were operated upon by the combined methods using a segment of jejunum for the lower part and a skin tube above

Such procedures, as Yudin describes, may be applicable for a carcinomatous lesion in the upper third of the esophagus, but are certainly not ideal for neoplasms of the middle or lower third of the esophagus If a one-stage procedure is used the patient would be subjected to an operation of tremendous magnitude In a two-stage procedure the patient would have to undergo the risk of a major operation before it is determined if the lesion is operable In addition, there is always the possibility of death of the jejunal transplant and/or infection of the subcutaneous tube

Construction of skin tubes, either with or without jejunal transplantation, usually requires numerous operative procedures Fistulae develop and strictures occur at the mucocutaneous junctions Both of these distressing complications are difficult to handle More than 50 per cent of

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anterior dermato-esophagoplasties are never completed, most of the patients dying of recurrence before the skin tube is completed

Recently, Garlock³ described a method for reestablishment of esophago-gastric continuity after resection of a carcinoma of the middle third of the esophagus. In his case he anastomosed the fundus of the stomach over and above the arch of the aorta. This procedure is a definite advance in the surgical treatment of carcinoma of the middle third of the esophagus. It not only affords radical removal of the tumor, but eliminates artificial swallowing devices or anterior thoracic esophagoplasties.

The success of Garlock prompted the author to attempt a similar procedure in a man who had a carcinoma involving the middle and lower thirds of the esophagus.



FIG 1—Roentgenogram of esophagus following ingestion of barium showing an irregularly stenosing filling defect which begins at the level of the 6th thoracic vertebra and extends to the diaphragm.

defect, suggestive of malignancy, involving the lower two-thirds of the esophagus (Fig 1). The chest showed no abnormalities.

Case Report—P. P., white, male, age 58, was admitted to the University of Chicago Clinics January 17, 1944. About four and one-half months before, he had noticed the onset of difficulty in swallowing meat and coarse foods. This difficulty gradually progressed, and for about one month prior to admission he could only take liquids, and even these were taken with difficulty. Solid foods would regurgitate almost immediately. He had some cough for two weeks, but there had been no change in his voice. Saliva would seem to accumulate in the upper esophagus and then he would have to "cough it up." He had no pain, but there was a sensation of food "sticking" in his throat. He had lost 29 pounds in weight and had become quite weak. Past history is not significant.

Physical Examination—The patient was a man of very small stature, somewhat emaciated, with evidence of recent weight loss. There were numerous carious teeth and marked pyorrhea. His voice was normal and he had no dyspnea. Lungs were clear. No cardiac murmurs. His blood pressure 102/70, pulse 75. Reflexes were equal and active.

Laboratory Data—White blood count 11,100, with a normal differential, hemoglobin 13 Gm., red blood count, 4,390,000. The urine was negative, blood chlorides 1025 mM/L, fasting blood sugar 75 mg per cent, plasma protein 6.38 Gm per cent, NPN 19 mg per cent. Electrocardiogram was essentially normal.

Roentgenologic examination following ingestion of barium revealed an irregular filling

TRANSTHORACIC ESOPHAGOGASTROSTOMY

At esophagoscopy, an ulcerating, friable mass, projecting into the lumen of the esophagus which bled easily, was seen. The lumen was considerably narrowed. A biopsy was made which subsequently revealed the lesion to be a squamous cell carcinoma.

Preoperative Preparation—The patient was in the hospital for one week prior to the operation, during which time he was given a high protein, high caloric diet supplemented with vitamins. Five days before operation he received 600 cc of whole citrated blood. He was slowly digitalized over a period of five days, and for four days before operation he received one gram of sulfadiazine four times per day.

Operation—January 24, 1944. Positive pressure ethylene-oxygen-ether anesthesia, administered through a snug-fitting face mask was employed. The patient was placed on his right side with the left arm suspended from a rectangular frame (Fig 2). A

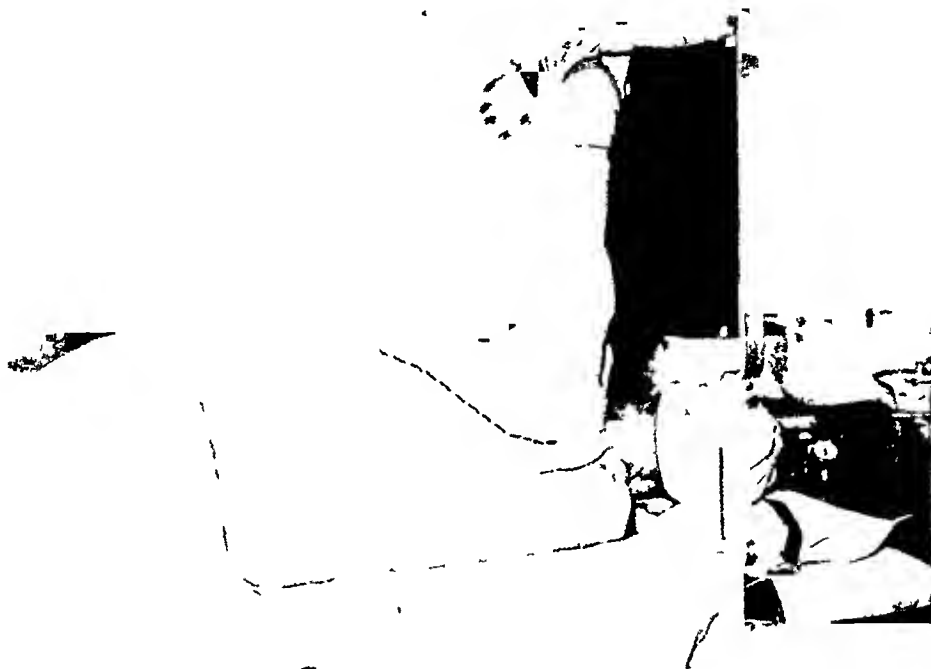


FIG 2—Photograph showing position of patient on the operating table. Dotted line indicates approximate skin incision.

long incision was made over the course of the seventh rib beginning at the costochondral junction anteriorly and extending backward to about the lateral edge of the recti spinae muscles. At this level it was carried upward for a distance of about 8 cm (Fig 2). The muscles were divided and the 7th rib exposed. At the posterior part of the wound the recti spinae muscles were reflected mesially exposing the posterior part of the rib and its accompanying transverse process. The entire rib was removed subperiosteally from its costochondral junction to the transverse process. The intercostal structures above and below the resected rib were divided between clamps near the transverse processes and ligated. The 6th and 8th ribs were transected about one inch from their accompanying transverse processes. The inner costal structures above and below these latter ribs were divided and the 5th and 9th ribs transected. This allowed the wound to be spread widely and afforded excellent exposure. The phrenic nerve was crushed just above the diaphragm. The esophagus, from just above the level of the arch of the aorta to just above the diaphragm, was involved in a very extensive neoplastic process. The mediastinal pleura was incised along the mesial edge of the aorta from the diaphragm to the arch of the aorta. By means of blunt and sharp dissection the esophagus was mobilized from the posterior mediastinum. This mobilization was begun just above the diaphragm and carried upward to the arch. Several adjacent firm, slightly enlarged lymph nodes were freed and left attached.

to the esophagus. Both vagus nerves were divided above the diaphragm. As the lower portion of the esophagus was freed, a small opening was made in the opposite mediastinal pleura. This did not seem to cause the patient any particular difficulty but did require a slight increase in the intratracheal pressure. At the arch of the aorta the esophagus was intimately adherent to the adventitia, trachea and left main bronchus. The mediastinal pleura was incised above the arch to the suprasternal notch. The esophagus above the level of the tumor was easily freed. By careful blunt dissection the involved esophagus was freed from beneath the arch of the aorta and from the trachea and left main bronchus. A portion of the adventitia was left attached to the esophagus. A 16-cm radial incision was made in the diaphragm from the periphery toward the esophageal hiatus. The left phrenic artery was divided and ligated. A mass of enlarged lymph nodes were found adherent to the left gastric artery near its origin. No other metastases could be seen or felt. The greater omentum was divided close to the stomach down to near the pylorus. This division was made so that the gastro-epiploic vessels remained in the omentum. The ligation was carried down to where the first branch of the right gastro-epiploic artery came off to the stomach. In order to remove the lymph node metastases it was necessary to divide the left gastric artery near the celiac axis. The upper and lower branches of the left gastric artery were divided and the gastrohepatic omentum incised near the liver. The lesser omentum, left gastric artery and its accompanying nodes were completely excised from the lesser curvature of the stomach. The stomach was divided just below the cardio-esophageal junction and the distal end infolded with two rows of linen sutures. The proximal end was covered with a rubber glove. The mobilized esophagus was then drawn out through the opening in the mediastinal pleura above and to the left of the arch of the aorta. The stomach, which appeared viable, was easily brought up into the chest and an anastomosis made between the end of the esophagus and an opening in the fundus of the stomach, with three rows of interrupted sutures of linen. The sutures were so placed that the esophagus was telescoped into the fundus of the stomach. The first posterior row of sutures was placed about 6 cm above the upper limits of the tumor. An umbilical tape was placed around the esophagus 3 cm above these sutures and tied twice, the second tie being a slipknot. The lower two-thirds of the esophagus was now removed and the anastomosis completed. There was no tension on the suture line. The elongated stomach was sutured to the pericardium and pleura over the aorta as far as the diaphragm which was closed with interrupted sutures around the prepyloric portion of the stomach (Fig 3). Five grams of sulfathiazole crystals were sprinkled in the operative field. A de Pezzar catheter was inserted posterolaterally through the 9th interspace for pleural drainage. The wound was sutured tightly. The defect in the posterior aspect of the wound, which is always difficult to deal with, was adequately closed by using the reflected recti spinae muscles. The intratracheal positive pressure was increased and the air aspirated from the pleural cavity through the de Pezzar catheter. During the course of operation, which lasted six and one-quarter hours 2400 cc of whole blood, 550 cc of plasma and 1850 cc of saline were administered. The patient stood the operative procedure very well.

Postoperative Course—Immediately after operation the de Pezzar catheter was attached to a modified double Wangenstein suction apparatus¹ and nasal oxygen started. The patient got along very well for six days, and liquids by mouth were started on the seventh day. He received 5 Gm of sodium sulfadiazine intravenously and one cent of digitalis intramuscularly daily. His temperature rose to 101° F on the second day and then gradually fell to normal by the sixth postoperative day. On the seventh day he became quite dyspneic, and examination revealed fluid in the right chest. Thoracentesis was performed and 2000 cc of chylous-appearing fluid was removed.

TRANSTHORACIC ESOPHAGOGASTROSTOMY

Cultures of the fluid were sterile, protein content 3.25 Gm per cent, total lipids 500 mg per cent. Following this, his dyspnea entirely disappeared, and he felt quite well. 2700 cc of similar fluid was removed from the chest on the following day. This, likewise proved to be sterile and had about the same protein content. On this day he was given 1100 cc of plasma to replace the protein loss in the fluid. On the ninth day he again showed signs of fluid accumulation in the chest and 1800 cc of chylous-appearing fluid was removed. This was given back to him intravenously without reaction. On the tenth day 440 cc of fluid were aspirated from the right chest and on this day the administration of sulfadiazine and digitalis were discontinued. By the eleventh day he was feeling fairly well and taking soft foods by mouth. He took food without difficulty in the upright position but when he was lying down he would choke, which was apparently due to accumulations in the thoracic stomach. He had a fairly good appetite and apparently had hunger pains. He was discharged on his twenty-seventh postoperative day.

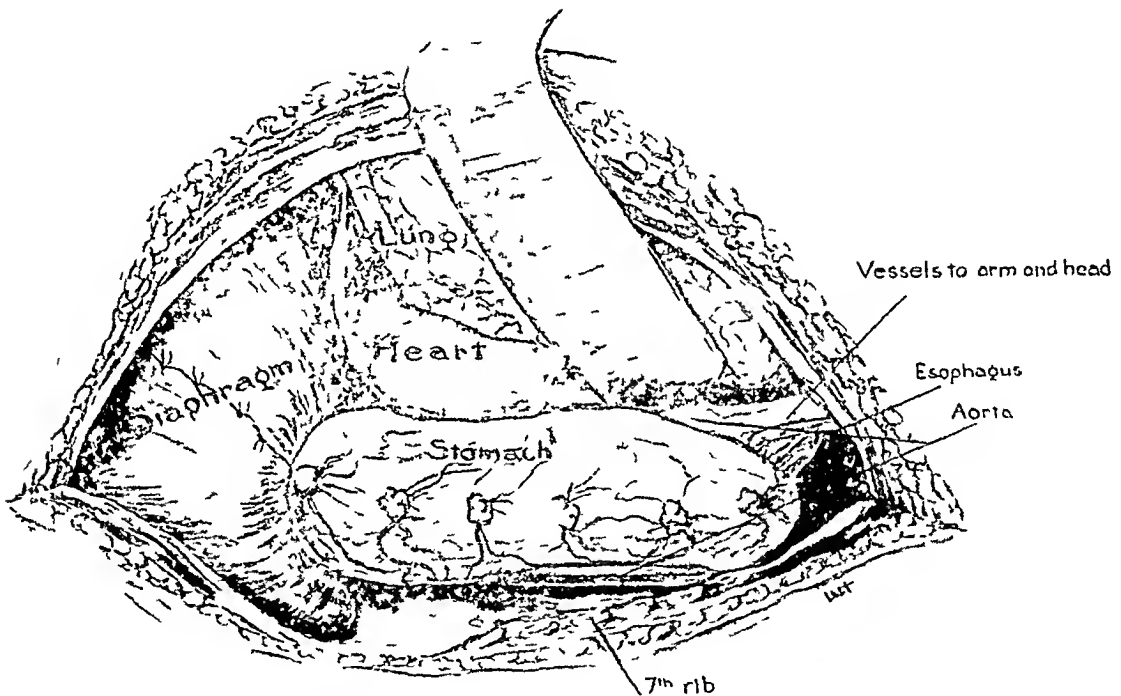


FIG 3—Shows the diaphragm closed around the prepyloric region and the elongated stomach anastomosed to the esophagus above the aortic arch. The stomach is drawn over the aorta.

An electrocardiogram taken ten days before his discharge showed no significant change from the preoperative tracing. Histamine test done three and one-half weeks postoperatively showed 78 clinical units of free hydrochloric acid in the 30-minute specimen. Roentgenologic examination after barium swallow, made two and one-half weeks postoperatively, revealed nearly all of the stomach in thorax and a well-functioning esophagogastrostomy (Fig 4).

The patient got along quite well for three and one-half months, then he began to lose weight and strength. A cough developed and his appetite failed. His condition gradually became worse, and he died June 23, 1944. Autopsy was not permitted.

Pathologic Report—Microscopic examination of the esophagus showed the lesion to be a squamous cell carcinoma. The mass of tissue removed from the lesser curvature of the stomach contained eight lymph nodes. Seven of these showed invasion of neoplastic cells.

DISCUSSION —Progress in esophageal surgery has not only been due to a better understanding of the physiology of the cardiorespiratory system, but also to improved pre- and postoperative care. Most of the patients when seen with neoplasms of the esophagus are elderly, dehydrated and under-nourished. Restoration of fluid and electrolyte balance as well as plasma protein level should be routine preoperative procedures.



FIG 4.—Roentgenogram of esophagus and stomach following ingestion of barium, two and one half weeks after resection and esophagogastrostomy. It shows nearly all of the stomach in the thorax. The anastomosis is at the level of the clavicles and the diaphragm is closed around the prepyloric region of the stomach. Fluoroscopy revealed no evidence of obstruction at this time.

Many of the patients who have been subjected to surgery of the esophagus have been given digitalis preoperatively. Although one cannot determine definitely when full digitalization has been accomplished we have administered an amount calculated on the basis of body weight. No adverse reactions have been observed, and the incidence of cardiorespiratory complications have been less in the cases where preoperative digitalization has been carried out. Garlock, in his case, divided only the upper branch of the left gastric artery.

He believed that if the main vessel was ligated the blood supply of the upper end of the stomach might be too seriously jeopardized. In the case reported herewith the greater and lesser curvatures were ligated off, down to the prepyloric region leaving only the blood supply which comes from the prepyloric segments of the right gastric and right gastro-epiploic arteries. Despite this extensive sacrifice of blood vessels the circulation of the stomach remained adequate.

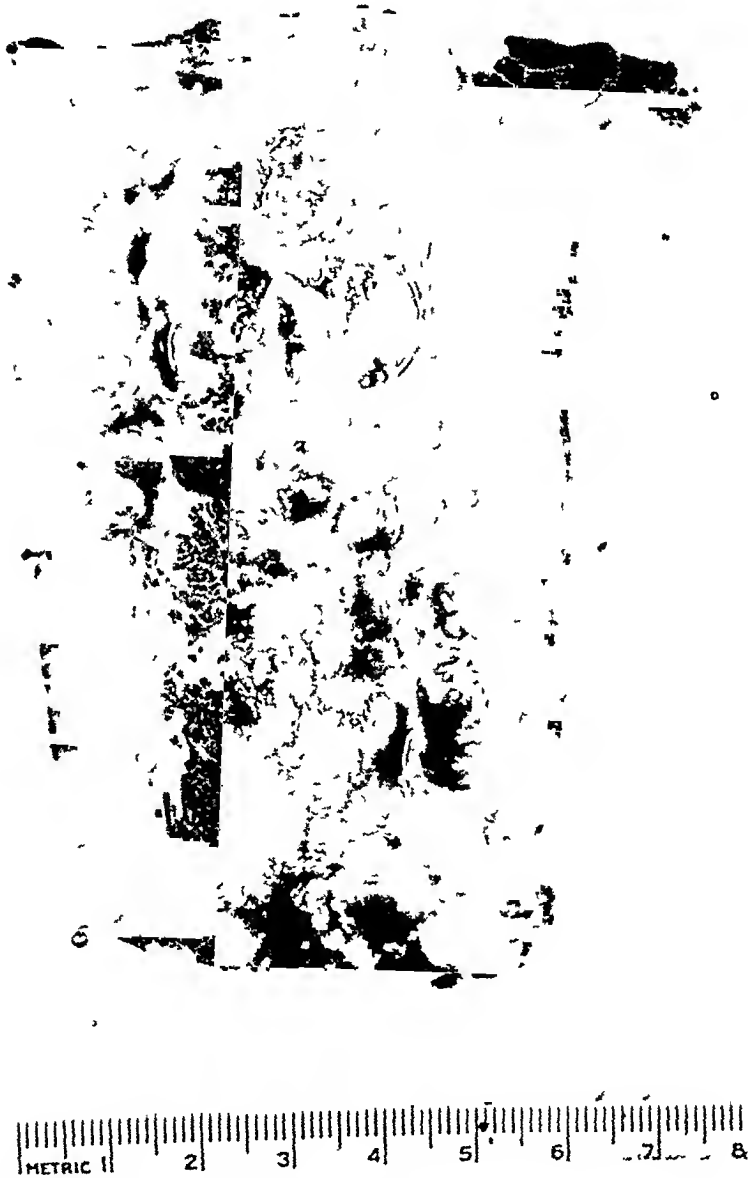


FIG. 5—Photograph of the resected specimen of esophagus. Note the extent of the lesion.

Ligation of the blood supply to such an extent presumably may result in necrosis of the stomach in some cases. Therefore, a safer procedure would be to leave the right and left gastro-epiploic vessels attached to the stomach, as shown in Figure 6, dividing and ligating the omentum distally. If this were done complete removal of the left gastric artery and its accompanying nodes could be performed with very little fear of impairment of gastric circulation. Since the lymph nodes along the lesser curvature of the stomach

are intimately associated with the lymphatic drainage of the esophagus, and usually contain metastases, their removal is absolutely indicated

For three and one-half months following operation the patient had very little trouble taking solid food providing he would eat in an upright position. Shortly after he began to lose his appetite he noticed that if he ate a moderate amount of food a sense of fullness would develop in the lower chest and epigastrium. He had some vomiting which gave relief. Roentgenologic study after the ingestion of barium, made at this time, revealed a marked

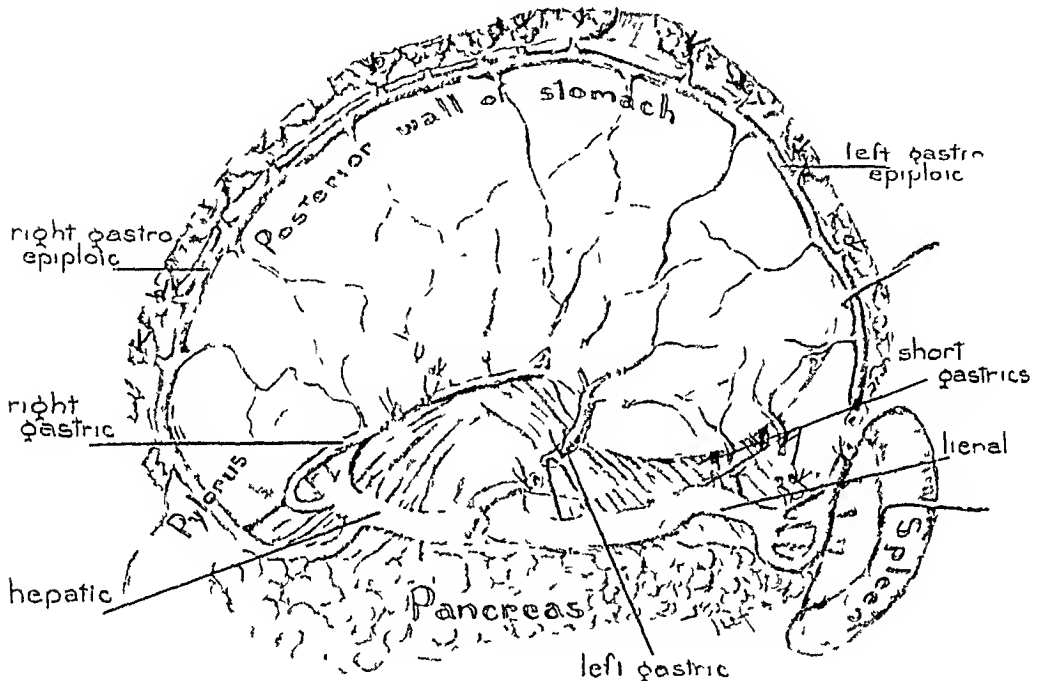


FIG. 6.—Diagram of the blood supply to the stomach indicating points of ligation of the vessels which would allow complete removal of the lymph nodes along the lesser curvature of stomach without fear of impairment of gastric circulation. The right and left gastroepiploic vessels are left attached to the stomach dividing and ligating the omentum distally. In the case presented the greater and lesser curvatures were ligated off down to the prepyloric region leaving only the blood supply which comes from the prepyloric segments of the right gastric and right gastroepiploic arteries.

obstruction of the stomach where it passed through the diaphragm. The excision of the left leaf of the diaphragm was full. It appeared that the obstruction was due to regeneration of the phrenic nerve and recovery of the muscle tone of the diaphragm. In view of this, it is a question, if it would not be better to excise a long segment of the phrenic nerve to insure permanent paralysis of the left leaf of the diaphragm. Many of the patients in whom part of the stomach has been transplanted into the chest complain of vague symptoms not unlike those of patients with diaphragmatic herniae. Permanent paralysis of the diaphragm may relieve or prevent many of these symptoms.

The patient's postoperative course was complicated by a chylous thorax. Because of the anatomic location of the thoracic duct the injury of it may be more frequent in resecting lesions of the middle third of the esophagus.

than in operations for lesions of the lower third. This complication has been observed now in two cases in this clinic. In both, the accumulation of chyle ceased spontaneously in three to four days. Since the protein content of chyle is about 2-4 grams per cent, depletion of the protein stores will occur very rapidly unless adequate replacement is promptly instituted. Plasma should be given or the chylous fluid, if sterile, may be administered intravenously. In the case reported, 4700 cc of milky fluid, with a protein content of 3.25 Gm per cent, was removed from the right chest on the seventh and eighth postoperative days. This protein loss was partially covered by the administration of 1100 cc of plasma. On the ninth day 1800 cc of similar fluid was obtained which was immediately administered intravenously, without any reaction.

Operations, such as the one described, are of tremendous magnitude, and the loss of blood is considerable in spite of careful hemostasis. If adequate blood and/or plasma replacement is carried out during the course of the operation the patients usually stand the procedure very well. Although this patient was a small man he was given 2400 cc of whole citrated blood and 550 cc of plasma during the operative procedure. There was no evidence of reaction from the citrate administered in the blood and plasma.

SUMMARY

1 A successful resection of a carcinoma of the middle third of the esophagus is reported. The esophagogastric continuity was reestablished by an anastomosis between the stomach and esophagus over and above the arch of the aorta.

2 A technic is suggested for preservation of the gastro-epiploic arteries which would allow complete removal of the left gastric artery and the lymph nodes along the lesser curvature of the stomach without fear of impairment of gastric circulation.

3 Certain aspects of the pre- and postoperative treatment are discussed.

4 Excision of a long segment of the phrenic nerve is recommended to insure permanent paralysis of the diaphragm.

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THE EFFECT OF CHEMOTHERAPY ON THE ILEUM SUBJECTED TO VASCULAR INJURY

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THE EXTENT to which intestinal flora aggravate the damage to the intestine inflicted by vascular injury has not been clearly demonstrated. The recent introduction of potent intestinal antiseptics,¹⁻⁷ succinylsulfathiazole and pthalysulfathiazole in particular, has made it possible to undertake such a study.

In a preliminary study Sarnoff and Poth⁸ found that succinylsulfathiazole conferred a protective effect upon a 50-cm segment of ileum with occluded venous return, by preventing perforation and permitting recovery of bowel integrity. In this report data is presented demonstrating the usefulness of chemotherapy in experimental venous obstruction and in strangulation obstruction of the ileum of the dog.

METHOD

In the morphinized dog under ether anesthesia a 50-cm loop of terminal ileum is exposed through an abdominal incision, with aseptic precautions. The accompanying mesentery is freed from adjacent mesentery by incision along its entire length from bowel to root of mesentery without injury to the vessels serving the rest of the intestine. All the veins in the isolated mesentery, which can be identified, are divided between ligatures. The division of the mesentery adjacent to the ends of the loop is carried to intestinal serosa, so that no identifiable vascular communication with adjacent loops remains. The incision is closed (Fig 1).

One series of dogs, Group I A, so treated, received no preoperative chemotherapy. Another, Group I B, received preoperative chemotherapy as follows. Of 16 dogs, seven received 0.5 Gm/Kg of succinylsulfathiazole daily in their food or by gavage,[†] and nine received 1.0 Gm/Kg of succinylsulfathiazole daily by gavage. Water was allowed postoperatively but food was withheld for 48 hours. All blood specimens were taken from the femoral artery. Hematocrit, plasma volume and plasma protein concentration were obtained immediately prior to venous occlusion and again 24 hours later.

The plasma volume was determined by the methods of Gibson and Evelyn,⁹ and of Gregerson and Gibson¹⁰ using the photo-electric colorimeter. Plasma protein concentration was determined from the plasma specific gravity (pycnometry method of Phillips, *et al*¹¹), and the conversion formula of Weech, *et al*¹².

* Three of these also received the drug in the same dose by gavage or in their food for two weeks postoperatively.

Autopsy was performed immediately after death or, in the case of surviving animals, after they were sacrificed at varying intervals post-operatively. Evidence was obtained on the source of collateral venous supply in the surviving animals and sections were taken for microscopic study.

When the venous return of a loop of ileum is treated as described, the following changes are observed. After five minutes cyanosis is obvious,

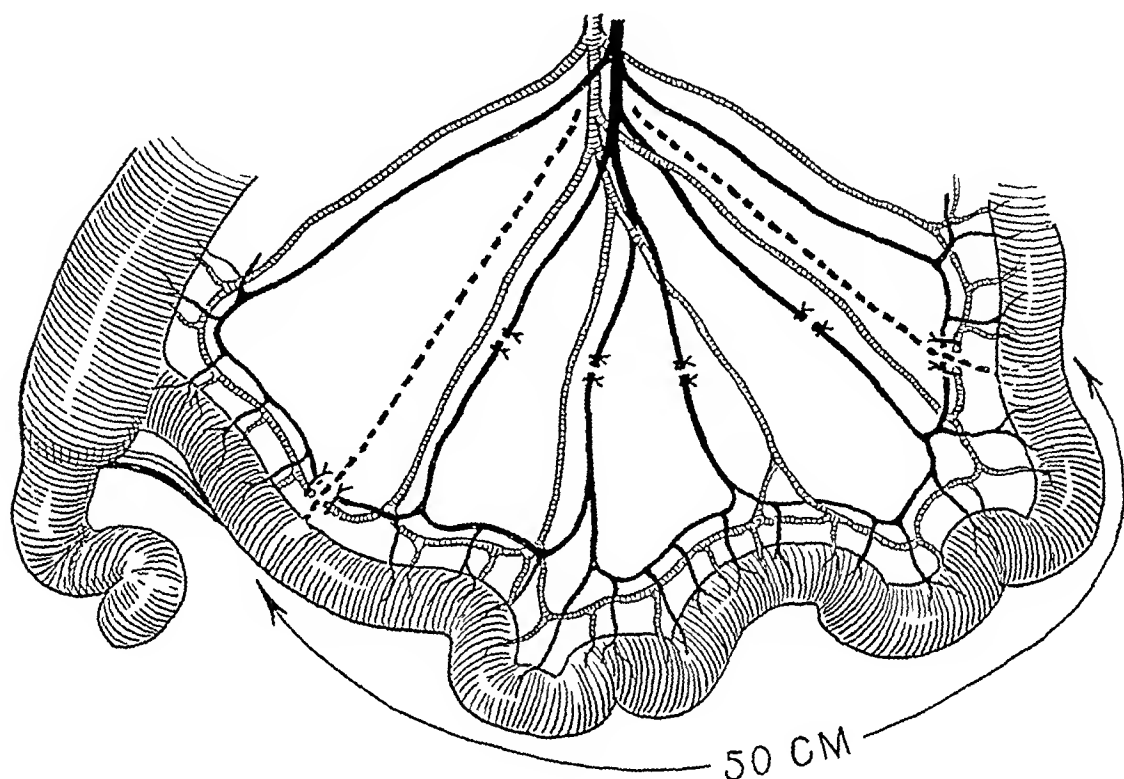


FIG. 1—Schematic diagram indicating procedure for occlusion of venous return of ileum

and after 15 minutes arterial pulsations disappear and the distended veins have pressures approaching the arterial diastolic pressure. After two hours the loop is deep purple, swollen and juicy, and the mesentery shows extravasation of blood as far proximally as the ligatures on the veins. The volume flow through such a loop approaches zero since, if exteriorized the temperature of the loop approaches that of the environment while adjacent loops are near body temperature.

In a second group of dogs, the foregoing procedure was repeated but the chemotherapy applied was as follows. Nine (Group II A) received succinylsulfathiazole locally (1.0 Gm/Kg), introduced at the time of operation by needle and syringe into the lumen just proximal to the loop and gently distributed in the area. No other chemotherapy was administered. In eight others, Group II B, the only chemotherapy administered was sodium sulfathiazole intravenously (0.1 Gm/Kg) immediately postoperatively and 0.05 Gm/Kg twice daily for one to two days thereafter.

In a third group (III) of 17 dogs, under evipal anesthesia, strangulation obstruction of a 35-cm loop of terminal ileum, exposed under aseptic precautions through an abdominal incision, was produced by tying a rubber



FIG 2—A Gross appearance of cross section of ileum after 24 hours of occlusion of venous return of ileum No enemotherapy



FIG 2—B Gross appearance of cross section of ileum after 24 hours of occlusion of venous return of ileum Succinylsulfathiazole by mouth for ten days prior of venous occlusion

band around the base of the loop so as to produce venous obstruction, as evidenced by cyanosis, without occluding arterial flow Twelve to fourteen hours later the incision was opened, under light ether anesthesia, and the rubber band released Many of the dogs, of course, showed evidence of shock All had copious bloody peritoneal fluid Nine dogs were treated immediately thereafter by an infusion of 5%-7% gelatin, in a volume equivalent to 60% of the dog's calculated blood volume The remainder were treated likewise, but they also received chemotherapy as follows One Gm/Kg of succinylsulfathiazole by syringe and needle into the loop proximal to the released loop and the same amount by mouth daily for two days thereafter, in addition sodium sulfathiazole 0.1 Gm/Kg was given in the gelatin infusion and 0.05 Gm/Kg intravenously twice daily for two days thereafter

TABLE I
SURVIVAL TIME FOLLOWING VENOUS OCCLUSION OF 50-CM LOOP OF TERMINAL ILEUM
Control Group Treated Group (see text)

Dog No	Survival Time in Hours	Sacrificed Days Postoper	Dog No	Survival Time in Hours	Sacrificed Days Postoper
1	47		1		15
2		23	2		22
3	40		3	42	
4		13	4		30
5	42		5		60
6	42		6		3
7	36		7		10
8	39		8	43	
9	84		9		6
10		10	10	24	
11	20		11		51
12	38		12		51
13	6.5 days		13		51
14	35		14		30
15	45		15	48	
16	37		16		30
17	37				
18	35				
19	12				
20	34				
21	30				
22	20				
23	40				
Average wt = 9.5 Kg Mortality 87%			Average wt = 9.3 Kg Mortality 25%		

RESULTS

Group I (Table I) Venous Occlusion With Preoperative Peroral Chemotherapy

In this group of dogs, with simple venous occlusion of a loop of ileum, 23 untreated control dogs (Group I A) showed a mortality of 87 per cent, death occurring in all but two of these dogs in less than 47 hours The group of 16 dogs receiving chemotherapy (Group I B), showed a mortality of 25 per cent within 48 hours The remainder survived and were sacrificed at intervals varying from 3-60 days postoperatively The surviving dogs lost weight, but appeared reasonably well and took food from the second postoperative day

In Table II data on changes during the first 24 hours postoperatively in blood and plasma volume, hematocrit and plasma proteins are listed. It is clear that no significant alterations occurred in these categories in both the treated and untreated groups of dogs. Therefore, when death occurred, it could not be attributed to shock resulting from blood loss arising from the vascular damage. The autopsy findings demonstrate that in the untreated group (I A) death was due to partial or complete dissolution of the loop, with resulting peritonitis. The four treated dogs which died differed from the untreated dogs in that no perforation was present. Nevertheless two showed gross evidence of peritonitis.

TABLE II
BLOOD CHANGES 24 HOURS AFTER VENOUS OCCLUSION OF ILEAL LOOP

Dog No	Blood Volume % Change	Plasma Volume % Change	Hematocrit % Change	Plasma Proteins % Change	Survival Time Hrs
Control					
8	-11.8	+6.4	-9.5	-10.0	39
9	-20.5	-22.8	-2.3	-15.0	84
10	-6.0	-3.0	-1.8	-13.9	s†
12	-23.6	-31.7	+5.2	+3.0	38
23	-4.8	-10.5	+3.0	0	40
—	—	—	—	—	—
Average	-13.3	-12.3	-1.1	-17.2	—
Treated					
5	-4.8	-12.2	+4.0	-8.5	s†
6	-12.8	0	-6.5	-8.0	s†
7	-10.5	-7.0	-2.1	-7.8	s†
8	-27.7	-17.5	-8.4	-11.1	43
9	-18.5	-14.4	-2.8	-8.0	s†
1†	-29.5	-26.7	-1.4	0	s†
2†	-25.2	-23.4	-2.5	-7.2	s†
3†	-11.3	+3.0	-7.0	-16.7	42
4†	-18.7	-21.7	+1.5	-1.3	s†
—	—	—	—	—	—
Average	-14.9*	-10.2	-3.2	-8.8	—

†s = Survived until sacrificed

† Preoperative blood volume estimated as 10% of the dog's weight in kilograms. Preoperative plasma volume calculated from preoperative blood volume and hematocrit.

* Calculated for Dogs 5-9 inclusive

Examination of the loops from surviving animals showed that venous collateral supply to the damaged segment was provided from three sources:

(a) The omentum, which was usually found adherent to the damaged segment.

(b) The mesentery of the damaged loop showed numerous functioning venous channels, evidently submacroscopic vessels, not detectable in the mesentery at the time of venous occlusion, which had become dilated.

(c) Adherent neighboring loops of bowel which oozed freely when separated. Gross inspection of the damaged loops at the time of sacrifice showed slight mottling, a somewhat larger luminal diameter, less active peristalsis than adjacent loops. The mucous membrane was intact and the mesentery showed some fibrosis.

Sections for microscopic study were taken at varying intervals after

operation in the treated group Examination of these sections yielded the following information

Twenty-four hours after operation Ulcerative necrosis of the mucosa with polymorphonuclear infiltration Tissue from submucosa to serosa hemorrhagic but relatively intact Process of repair evident in deep portion of mucosa and in muscularis Lymphatics distended Arteries contracted No bacteria seen

Three days after operation Massive hemorrhage into the mesentery, the entire muscularis and between mucosal glands and muscularis mucosae Superficial portion of the villi edematous In places superficial necrosis of the mucosa and replacement with granulation tissue Fibrin deposits on the serosa Almost complete absence of thrombosis

Six days after operation Hemorrhage into mesentery and the muscularis Fibroblasts and lymphocytic infiltration of the mesentery and submucosa The venules and capillaries of the submucosa distended Extensive slough of mucosa with granulation tissue replacement Fibrin deposits on thickened serosa No evidence of thrombosis

Ten days after operation Fibrosis, and lymphocytic infiltration of the mesentery, thickening and lymphocytic infiltration of serosa The mucosa, submucosa and muscularis are not remarkable

Twenty-two days after operation Lymphocytic infiltration of mesentery Occasional organized mural thrombus in mesenteric veins Intestine otherwise normal

Thirty days after operation Except for some thickening of the serosa at the site of adhesions and some fibrosis in the mesentery, tissue is indistinguishable from normal bowel

TABLE III
EFFECT OF CHEMOTHERAPY ON MORTALITY AND PERFORATION FOLLOWING VENOUS OCCLUSION
OF A 50-CM LOOP OF ILEUM

Group	No of Dogs*	Mortality Rate	Perforation Rate in Animals that Died
I A No chemotherapy	23	87%	75%
II A Intraluminal chemotherapy at time of venous occlusion (succinylsulfathiazole)	9	66%	0
II B Intravenous chemotherapy for 24-48 hours following venous occlusion (sodium sulfathi- azole)	8	50%	0
I B Preoperative chemotherapy (succinylsulfathi- azole)	16	25%	0

* Average weight in different series 9.3 - 10.4 Kg

Group II Venous Occlusion With Simultaneous Chemotherapy

(A) *Local Instillation of Succinylsulfathiazole* Of nine dogs in this group (II A, Table III) six succumbed in under 48 hours There were no perforations, however, in any of these six animals, although in two the wall was quite thin and gross peritonitis was present The remaining three survived, and showed the gross findings already described for survivors in Group I B

(B) *Intravenous Sodium Sulfathiazole* Of eight dogs (Group II B, Table III), which received intravenous therapy as described, four died, but, as in the locally treated group, no perforations were present. The remaining four survived and showed, when sacrificed, the usual findings seen in surviving animals.

Group III Strangulation Obstruction

Of nine dogs with strangulation obstruction (released after 12-14 hours) which received an adequate volume of a blood substitute (gelatin) but no chemotherapy, none survived, death occurring from gangrene of the loop and diffuse peritonitis. Survival was less than 20 hours after release of the strangulation in all but two, which survived six days. In the latter two autopsy showed peritonitis but no obvious perforations, the remainder showed perforations.

Of a similar series of nine dogs, which received chemotherapy as described, three survived and six died. Two of the six which died showed perforations and peritonitis at autopsy, a third showed peritonitis too but no perforation, the loop having apparently recovered, two more showed no perforation but gangrene was present, while the sixth showed neither, and died of bilateral pneumonia. Of the nine treated dogs, therefore, the chemotherapy prevented death in three, perforations in seven and peritonitis in five. The survival time in the five which died was 2, 4, 4, 2 and 5 days as compared to an average of 20 hours for the dogs not receiving sulfonamides. The three surviving dogs showed a remarkable degree of recovery of the loop. All layers of the intestine showed a somewhat dusky, deep brownish-red discoloration, there was slight edema of the mucosa which, however, was intact throughout. The mesentery was slightly cloudy and thickened, and the serosal surface of the intestine showed patches of fibrin in addition to easily separated adhesions between adjacent surfaces. The only evidence of ileus was very slight dilatation of the proximal intestine in a few of the dogs. The vascular supply to the loop was apparently normal by gross inspection.

In view of the fact that the loop in 87 per cent of the dogs not receiving sulfonamides showed partial to complete necrosis, the protective effect of chemotherapy is obvious.

DISCUSSION—Numerous quantitative studies^{13, 14} have demonstrated that severe vascular damage to the intestine can be rapidly fatal from loss of blood volume alone. For the clinical surgeon, the therapeutic problem, therefore, is made somewhat less difficult by the provision of blood volume replacement. But the primary lethal factor of secondary infection through a permeable bowel wall remains so that resection not only of devitalized but of questionably viable loops constitutes a cardinal principle in the surgical treatment of strangulation and of mesenteric thrombosis.

The remarkable feature of sulfonamide action in the experiments de-

scribed is their apparent ability to forestall complete necrosis. Presumably, they do so by suppressing the thrombotic action of tissue juices or bacterial products in an area of threatened devitalization and so allow time for effective collateral supply to become established. The microscopic evidence in surviving animals is that remarkably little thrombosis is evident in the obstructed veins, whereas in the one microscopic section of an early stage in the rapid disintegration of a loop in an untreated dog, thrombosis of the veins was widespread.

There is no evidence to assume that the protective effect of the sulfonamides in these experiments is achieved by any other mechanism, *e g*, one which might directly or indirectly prevent a substantial fall in blood volume. No significant fall in blood or plasma volume was observed in treated or untreated dogs with simple venous occlusion, while in strangulation obstruction the loss in blood volume was adequately replaced in the treated and untreated series. Advance chemotherapy might have provided for more protection than was obtained in these strangulation experiments. But while such data should be secured, they have little practical bearing on the clinical problem of strangulation, since it is not a condition that can be anticipated.

The foregoing experiments suggest the potentialities of sulfonamide therapy. The maximal effect possible with the relatively insoluble sulfonamides can be secured in elective bowel surgery. Since they require at least several days to produce a substantial bacterial depopulation of the intestine, their administration would not be appropriate in acute conditions in which vascular damage is already present, unless peritonitis may be anticipated, *e g*, in incomplete, but diffuse, mesenteric thrombosis, in which viability is problematical and in which resection is not advisable because of too extensive involvement of the intestine. The soluble sulfonamides have a certain limited usefulness at, and subsequent to, the time of operation for a strangulation, which is released but not resected, as the experiments of Groups II and III indicate, since perforation is frequently avoided by their use. Their administration in conjunction with the local instillation of the less soluble sulfonamides may be of not inconsiderable value in elective bowel surgery. For if a point in a suture line becomes partially devitalized because of a technical error or an unavoidable postoperative complication, the threat of peritonitis may be forestalled if bacterial permeation is kept to a minimum by these agents.

CONCLUSIONS

- 1 The lethal effect of the simple vascular occlusion produced in these experiments is not attributable to a crucial fall in blood volume, but to peritonitis with, or without, gross perforation.

- 2 The protective effect of succinylsulfathiazole is maximal when applied well in advance of production of the vascular injury, while chemotherapy at

the time of, or subsequent to, the production of the vascular injury is also effective but to a distinctly lesser extent than advance chemotherapy

3 The data suggests the probable usefulness of chemotherapy in corresponding clinical states in man

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DIVERTICULITIS OF THE CECUM A METHOD OF MANAGEMENT

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DIVERTICULITIS OF THE CECUM is rarely included in discussions of diverticulitis of the colon since the former is characteristically solitary and appears to be a distinct entity. In recent years the subject has received considerable space in the literature. Schnug,¹ in 1943, reviewed 31 cases and added six of his own. In 1938, Bennett-Jones² had been able to collect but 19 cases to which he added three.

Most cases of diverticulitis of the cecum occur before the age of forty, and one-third of the cases have had previous attacks. Almost invariably, the preoperative diagnosis is acute appendicitis. Rarely is the diagnosis of diverticulitis made before celiotomy.¹

At operation one may encounter a pericecal mass which is recognized as inflammatory, and palpation through the opposite cecal wall may reveal the mouth of a diverticulum. Often an inflamed or gangrenous diverticulum is obvious. Sometimes, the pathologic process becomes so tumefied and involved with enlarged mesenteric lymph nodes that the surgeon thinks he is dealing with a malignant tumor.

From the reviews,^{1, 2} and from the case reports,^{3, 4, 5, 6} it is evident that agreement as to the most satisfactory surgical approach has not been reached. Schnug advised chemotherapy without attempt at resection, on the basis of the tendency for the lesion to drain into the bowel and subside. Jonas reports that it has been their practice to resect the entire right colon and cecum with an ileo-transverse colostomy. Others recommend conservative surgery from simple drainage to local excision of the diverticulum and closure of the cecum.

The edema and thickening of the surrounding cecal wall make local excision of the diverticulum difficult and closure hazardous. This is true whether the diverticulum be mildly inflamed or strangulated, and with or without an attached inflammatory mass or abscess. To resect a large segment of the bowel for so benign a lesion seems most radical. On the other hand, to close the abdomen without attempting to eradicate the lesion and thus chance perforation challenges one's courage.

Case Report—Hosp No 28696 Age 37 The patient was well until the day before admission when he experienced epigastric discomfort which later shifted to the right lower quadrant. There was no nausea, vomiting or diarrhea. On the morning of admission, the pain was more severe and was accompanied by anorexia. On physical examination, there was moderate tenderness in the right lower quadrant, maximum to the right of McBurney's point. A minimal amount of muscle spasm was present, and upon hyperextension of the right thigh, the abdominal tenderness became more pronounced. Rectal tenderness was absent. The leukocyte count was 12,800, with 77 per cent polymorphonuclears, 19 per cent lymphocytes and 4 per cent monocytes. Hemo-

globin was 14 Gm. The uranalysis was negative. *Clinical Diagnosis* Acute appendicitis, probably retrocecal in position.

Operation—Under spinal procaine anesthesia, later supplemented by intravenous sodium pentothal, the abdomen was opened through a conventional McBurney incision. A mass was felt in the posterior wall of the cecum which, after delivery into the wound, had the appearance of a neoplasm, incorporated in the cecal wall (Fig 1). No crater was felt by palpation through the wall of the cecum. The serosa was divided and dissected off the tumor to its periphery where it appeared to diffuse with edematous



FIG 1—Schematic drawing of ileocecal region indicating the relative size and position of tumor of cecum.

cecum (Fig 2 A). An incision was made into the tumor for biopsy, and upon incising for a depth of about seven millimeters a firm black mass was encountered (Fig 2 B). The hard shell was further incised and dissected from the new structure, which, when completely exposed, appeared as a gangrenous mass surrounded at its base by normal mucosa (Fig 3 A). It was then apparent that the mass was a strangulated diverticulum. The granulomatous tissue, covering the diverticulum, was cut away, and the peritoneum was sutured to the serosa and thickened wall of cecum around the diverticulum (Fig 3 B). The remainder of the wound was packed with vaselined gauze and, thus, the diverticulum was exteriorized.

Fecal material began to drain from the wound on the third day, and the patient's condition was good throughout a relatively uneventful convalescence. Two weeks

DIVERTICULITIS OF CECUM

after operation he began to have formed stools per rectum. However, drainage from the wound persisted for a prolonged period, presumably due to the inflammatory state of the cecum. Barium enema showed a persistent small fistula, but otherwise, a normal colon without deformity of the cecum. Slight soiling of the dressing is still present at the time of this report, 45 days after operation.

DISCUSSION—The mass encountered was incorporated in the wall of the cecum and covered by normal serosa (Fig 1). There was striking absence

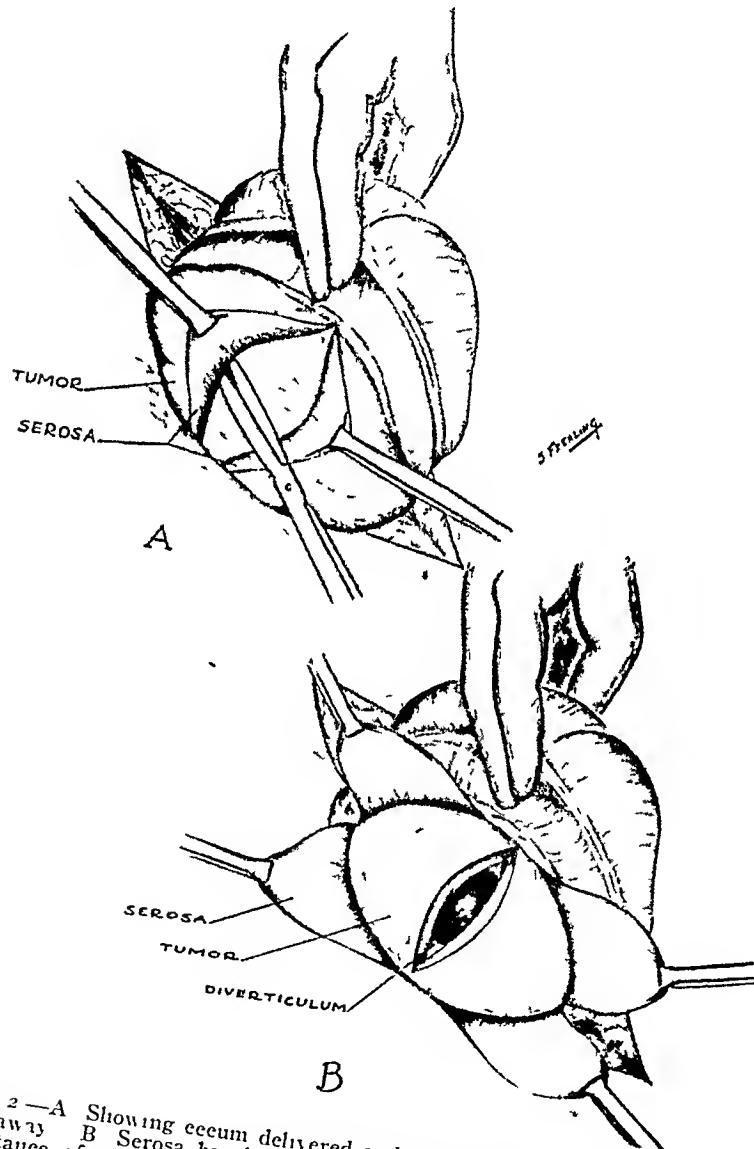


FIG 2—A Showing cecum delivered and serosal covering of tumor being stripped away. B Serosa has been stripped to periphery of tumor. Incision into substance of tumor reveals trapped diverticulum.

of any inflammatory adhesions. The tumor had the gross characteristics of neoplasm, and a Mikulicz resection was contemplated until the diverticulum was actually exposed during the procedure of securing a biopsy of the tumor. It would have been impossible to excise the lesion without removing an excessive amount of colon. The large portion of cecum which made up the mass was greatly thickened and hard (Figs 2 and 3), and the remaining cecal wall was edematous.

To leave a gangienous diverticulum, particularly after it had been exposed, would violate the principles of good surgical judgment. Subsequent perforation would be disastrous. Extrapertonealizing the immediate site of the diverticulum, thus sealing the peritoneum around its base, assures an uncomplicated cecostomy. In 48 to 72 hours the gangienous diverticulum will slough or can be opened very simply.

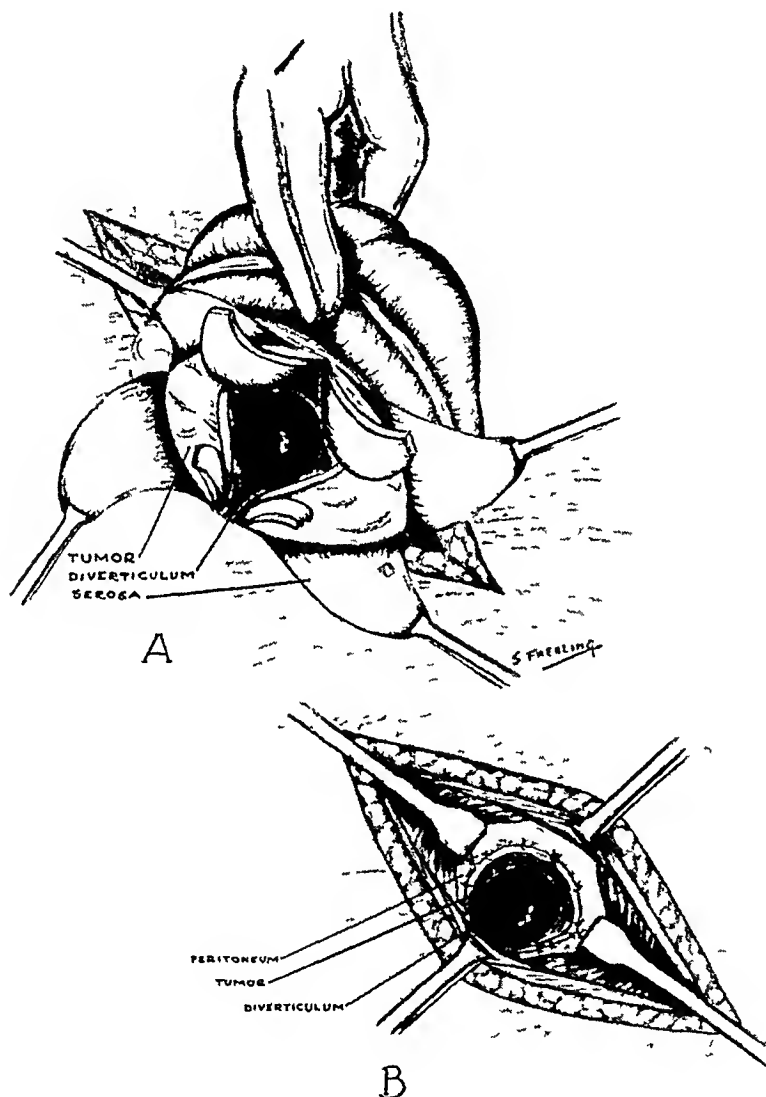


FIG 3—A Incision into tumor extended and granulomatous wall dissected away from diverticulum. Normal mucosa surrounds base of diverticulum. B The granulomatous wall has been cut away, and the cecum returned to the peritoneal cavity. The peritoneum has been sutured to the granulomatous wall of cecum around base of diverticulum.

In the absence of obstruction, the fistula should close spontaneously. The time required for this will undoubtedly depend upon the amount of inflammatory thickening of the cecum. It is possible that occasionally secondary closure of the cecum will be necessary.

It seems that the procedure described is applicable to most instances of

diverticulitis of the cecum, unless perforation and abscess formation have taken place. Obviously, these cases should be drained.

SUMMARY

- 1 The diverticula of the cecum are characteristically solitary
- 2 At operation, many are mistaken for a malignant tumor of the cecum because of accompanying inflammatory mass
- 3 The literature on the subject displays a variance of opinion as to the best surgical approach
- 4 A case is presented, and illustrated, to demonstrate the difficulty in recognizing the pathology and the corrective procedure employed
- 5 Extraperitonealization of the immediate site of the lesion as a prececostomy is suggested as the ideal method of management in most cases of solitary diverticulitis of the cecum

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MULTIPLE POLYPOID DISEASE OF THE COLON AND RECTUM

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THE EXTRAORDINARY CONDITION variously termed by different writers polyposis, polypoidosis, multiple adenomatosis or multiple polypoid disease of the colon is a malady *sui generis*, and is distinctly different from cases of single or multiple polypi resulting from irritative or infective influences

Virchow,¹ in 1863, first described this curious and rare disease, and in 1882, Harrison Cripps² reported a case. All of the literature since the publication of the latter until 1930 was reviewed by Cuthbert Dukes³ in the Cancer Review for April, 1930. During the intervening years to date, reports of single or small series of cases have appeared in the literature from time to time. In 1942, C W Mayo⁴ reported that in postmortems of 334 patients who had died of primary carcinoma of the colon or rectum, eight showed multiple polypi. The senior author saw only two such cases on the rectal and colon service at the U S Naval Hospital, Philadelphia, during a three-year tour of duty, 1937-1940. One of these patients had developed two separate and distinct malignancies in his colon prior to the time of his reporting to the hospital. The junior author has seen two cases of hereditary familial multiple polypoid disease in his private work—a mother, age 60, and her daughter, age 25, both of whom died of extensive carcinomatosis. Buie,⁵ in reviewing his series of 1234 cases of polypoid disease seen over a nine-year period, that is, 1925-1934, broke this series down into three groups as follows:

Group I One or only a few polypi—1069

Group II Multiple polypi associated with inflammatory disease of the colon—110

Group III Multiple polypoid disease of the entire colon—55 (or 4 per cent of the entire series)

McLaughlin,⁶ in 1943, stated that 331 cases had been reported in the literature since Virchow's original report in 1863.

The disease, although occurring infrequently, is of great importance because of its proximity as a relentless killer. Those so afflicted are almost certain to die of cancer at an early age unless radical surgery is instituted early. It is a familial or inheritable disease transmitted by both sexes and attacking both sexes. It appears to behave as a mendelian dominant.

J P Lockhart-Mummery,⁷ of St Mark's Hospital, London, points out that an interesting feature of the disease from the standpoint of its being hereditary is that it differs from most hereditary diseases such as hemophilia, albinism,

deaf-mutism, *etc*, in the respect that children are not born with it but tend to develop the condition about the time of puberty or during early adult life. In a few cases it may not develop until early middle age. On this score it is similar to hereditary amaurotic family idiocy, or hereditary optic atrophy.

In his classical discourse on the origin of cancer, Lockhart-Mummery has gone on to contend that in the light of our recent knowledge of biology a veil has been lifted and that the way may soon be clear to an establishment of the fact that many diseases of hitherto unknown origin may be shown to have as an underlying or antecedent factor this same kind of genetic background.

The crux of the whole matter is held to depend upon the tendency towards a genetic mutation of somatic cells. Just where the mutation started is difficult in most instances to say. In the case of hemophilia, it seems fairly certain that it began in some ancestor of the Coburg royal family several hundred years ago. In adenomatosis, as in other diseases of genetic origin the results of a mutation of the genes may appear in succeeding generations either as dominants or recessives, if as a mendelian dominant, the disease will tend to occur in every generation. This is true of adenomatosis. If the condition is a recessive it will be necessary for both parents to carry the mutative genes. This may not occur for a great many generations and the hereditary factor will consequently in all probability not be recognized.

It appears reasonably clear in adenomatosis that the hereditary factor consists of the tendency of the epithelial cells of the large bowel to proliferate. This occurs in the majority of cases at an early age and results in the development of countless simple adenomata, any and all of which carry the potentialities of developing, with time, into an adenocarcinoma by reason of further imposed mutation of its component cells.

This explanation may seem fantastic to some, and to fall into a category belonging to the realm of logomachy. In any event, the two important facts which seem to have been conclusively proven and which must be accepted are that first, adenomatosis or multiple polypoid disease of the colon is an inheritable condition, and, second, that malignant supervention is inevitable at an early age in practically 100 per cent of such cases. The first of these truths constitutes a distinct indication for investigating other members of a family, one member of which is found to be so afflicted. The second constitutes a justification for the institution of such a formidable operative procedure as total colectomy which was done in one of the cases here reported (Figs 3 and 4).

When the polypi in the rectum and rectosigmoid are not too numerous to permit their removal by fulguration through a sigmoidoscope certainly the operation of choice is to perform a side-to-side ileosigmoidostomy, as a first stage and several weeks later a resection of the short-circuited large bowel as the second stage of a two-stage operation. This was done in the second case of our series (Figs 8 and 10).

While proctosigmoidoscopic examination will reveal the presence of

polypi in the majority of instances, no patient should be considered conclusively examined until a roentgenologic study of the colon has been made. The importance of a contrast film following the injection of air after the barium has been evacuated cannot be overemphasized. This fact is strikingly revealed by the roentgenograms shown in connection with this report (Figs 1, 2, and 7a, b and c)

CASE REPORTS

Case 1—K C W, age 28, a Water Tender First Class, was admitted to the proctologic service of the U S Naval Hospital, San Diego, Calif, March 1, 1943, with an established diagnosis of hemorrhoids.

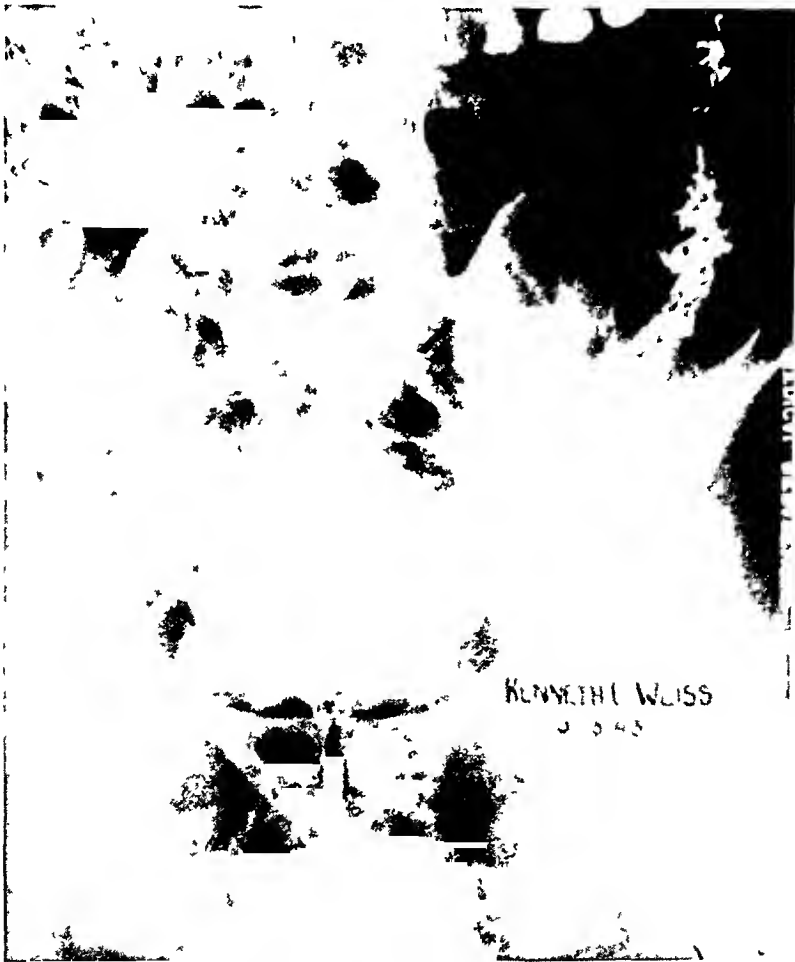


FIG 1—Case 1 (K C W) Roentgenogram of large bowel showing partial evacuation of cecum. Adenomatosis indifferently shown.

The patient had noticed occasional bleeding from the rectum, and the occasional protrusion of a soft mass from the anal outlet for a period of ten months. During the past two years he had passed four to six soft to watery stools daily.

On digital examination of the rectum there was noted a soft, polypoid mass on the anterior wall of the lower third of the rectum. Proctosigmoidoscopy to a distance of 24 cm revealed numerous polypi and polypoid masses, small to medium size, as far as examined. No normal looking mucosa was seen. Specimens of tissue were obtained for microscopic study. General physical examination showed nothing abnormal.

Roentgenologic studies of the upper gastro-intestinal tract were negative. The roentgenologist's report of his study of the colon is quoted in full.

"Roentgenologic examination of the large bowel by barium enema shows no delay to the passage of barium. However, there are numerous smooth, intrinsic filling defects visible throughout the colon from the rectum to the cecum. These measure about 0.5 to 1 cm. in diameter and appear to be in proximity to one another, so that almost the entire mucosa is involved. There is very little normal intervening mucous membrane.



FIG 2 —Case 1 (K C W) Following inflation of colon with air, extensive polypoid disease is revealed

"Films taken after the evacuation of barium and following the introduction of air into the bowel show the above described polypi to involve the entire mucosa of the colon (Figs 1 and 2).

"Impression Polyposis of the entire colon"

The diagnosis was changed from hemorrhoids to polypi, multiple, colon

The Tumor Board, upon reviewing this patient's problem, concurred in our recommendation that a complete colectomy be performed.

On May 10, 1943, a single-barrel ileostomy was established under spinal anesthesia supplemented by intravenous anesthesia (sodium pentothal). Convalescence was rapid and uneventful (Fig 5).

On July 17, 1943, the second stage was undertaken. The large bowel was removed, including ileal stump, cecum, ascending, transverse, descending, and sigmoid portions of the colon as far as the rectosigmoid. The rectosigmoid was left buried beneath the reconstructed pelvic floor. A drain left in the hollow of the sacrum was brought out through a stab wound near the tip of the coccyx. Ten grams of sulfanilamide were placed in the coelomic cavity. Anesthesia comprised continuous spinal and intravenous sodium pentothal.

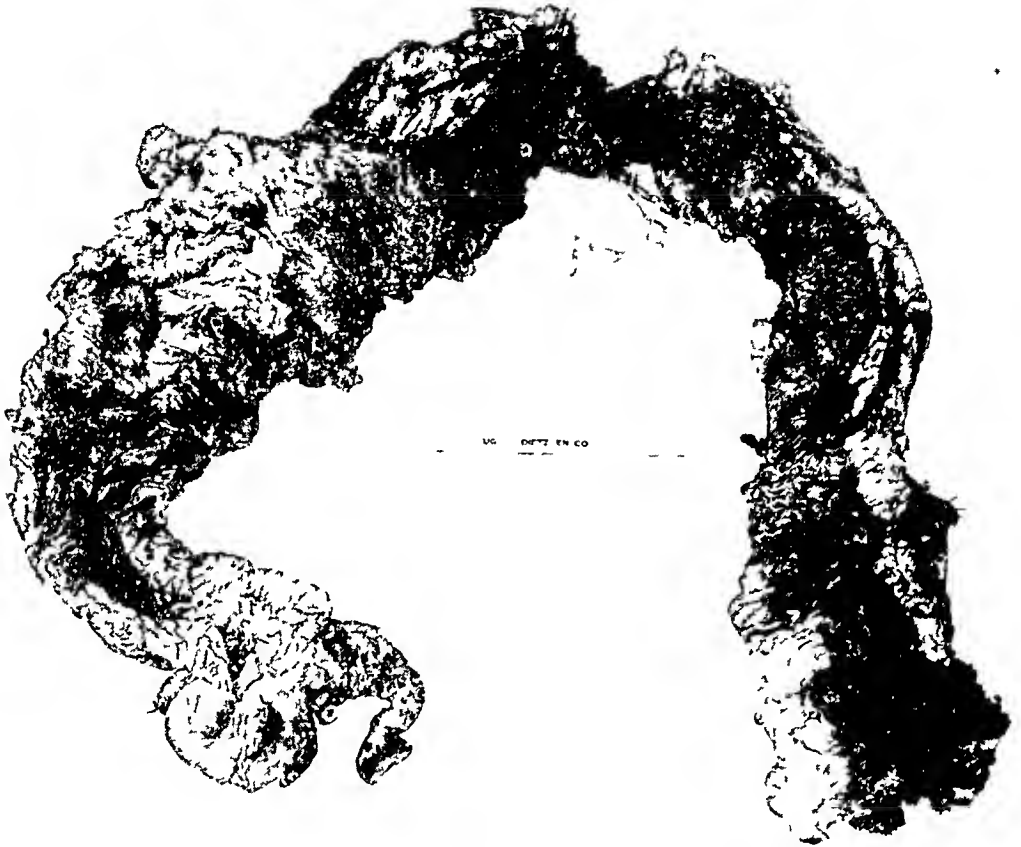


FIG. 3—Large bowel. Case 1 (KCW). Mucosa was studded with myriads of polypi, however, photographic scale is too small to show individual lesions.

Convalescence from this extensive procedure was uneventful until July 31, 1943, when the patient developed severe abdominal cramps and pain. The ileostomy suddenly ceased functioning. Attempts to pass a Miller-Abbott tube beyond the stomach were unsuccessful. Roentgenologic examination of the abdomen was suggestive of intestinal obstruction.

On August 1, 1943, an exploratory celiotomy was done and a loop of ileum was found adherent to the parietal peritoneum in the right upper quadrant and obstructed. A small abscess was discovered at the site of obstruction. The adherent bowel was freed, a cigarette drain was placed through a stab wound, and sulfanilamide crystals were placed in the abdominal cavity. Convalescence from this emergency procedure was uneventful.

On September 2, 1943, several small sessile polypi in and about the ileostomy stoma were destroyed by means of fulguration. The terminal ileum was examined to a distance of 14 cm by means of the small caliber proctosigmoidoscope. No other polypi were noted.

On October 7, 1943, the final stage was undertaken—a perineal excision of the rectosigmoid, rectum, and anal canal (Fig 4). Technically, this was indeed difficult because of the unusually long period of time between the second and third stages, occasioned by the surgical treatment of the acute intestinal obstruction.

All specimens were examined carefully. The pathologist reported no evidence of malignancy.

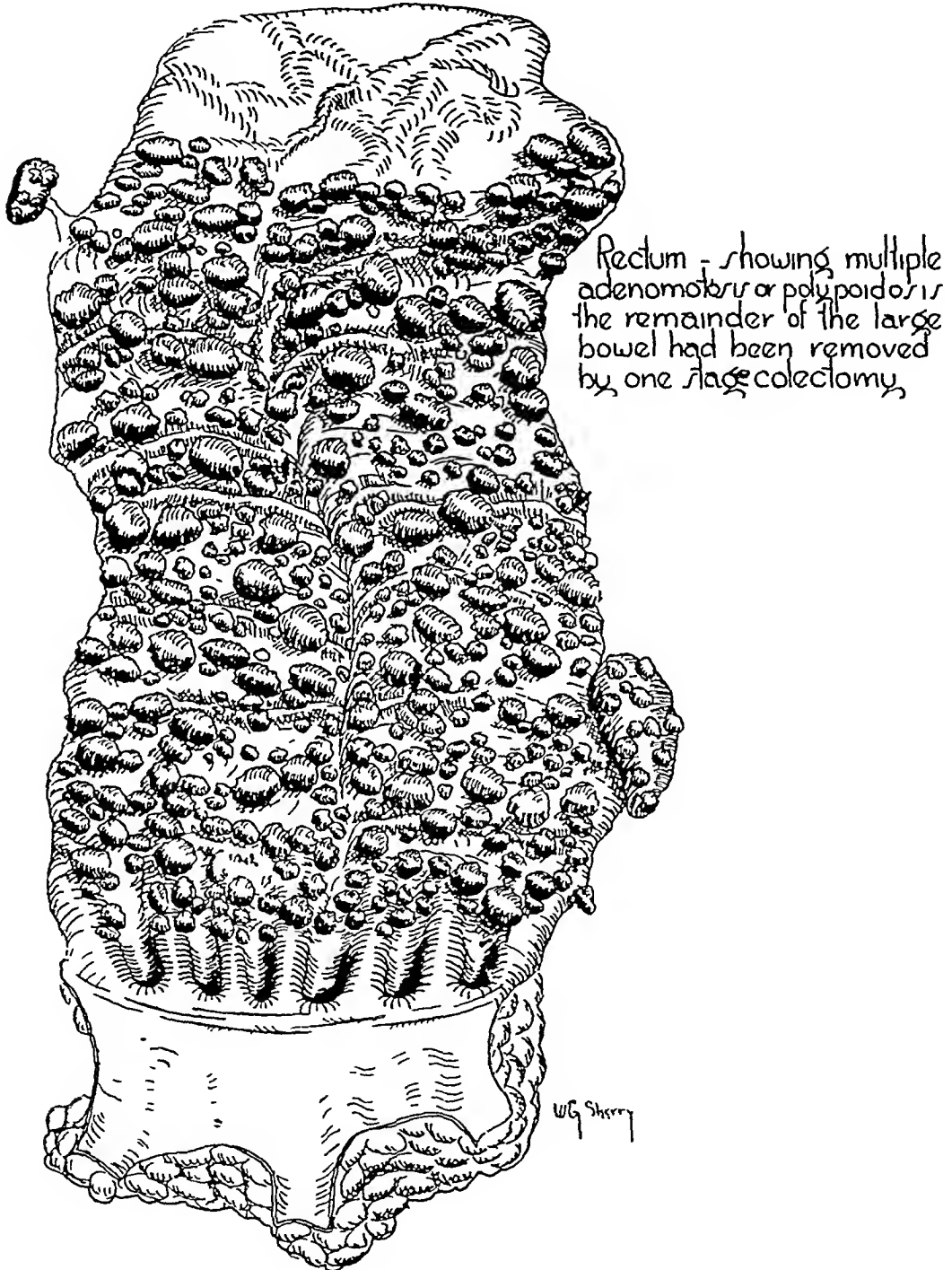


FIG 4—Pen drawing of rectum, Case 1 (K C W) Showing multiple polypoidosis

The patient's convalescence was satisfactory following the perineal excision. The perineal wound healed completely and bladder function was normal. He was ultimately discharged to limited duty wearing an ileostomy bag. There was no skin irritation around this ileostomy (Fig 5) and the intestinal excreta had become semisolid in

consistency The manner in which this patient became reconciled to his ileostomy and adapted himself to the use of an ileostomy bag was indeed gratifying

This patient presents an interesting and suggestive family history (Fig 6) We should like an opportunity to examine the three sisters who are said to be living and well, such examination has been advised

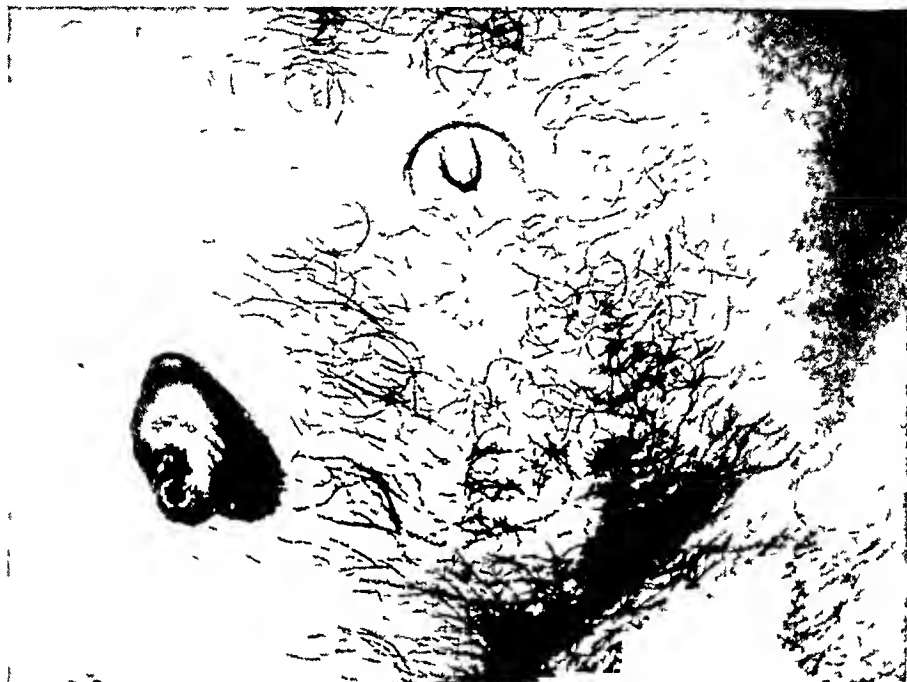


FIG 5—Case 1 (K C W) Single barrel ileostomy

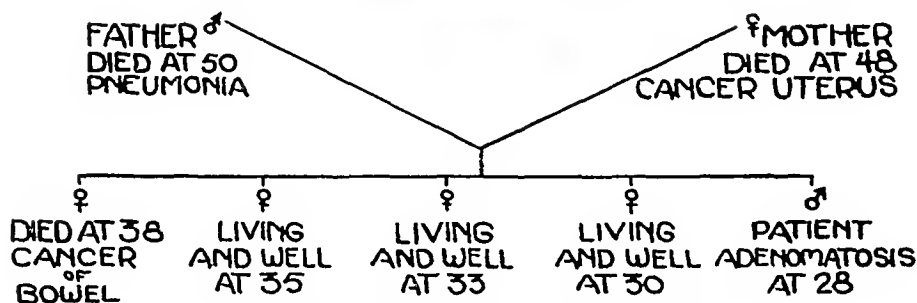


FIG 6—Diagram of family history of Case 1 (K C W)

Inasmuch as the patient is married the question arises as to the advisability of his having children, in view of the mendelian possibility of his offspring developing polypoid disease of the large bowel

We believe that this patient is permanently cured and that several factors have contributed to the successful outcome (1) It was fortunate that the patient's polypoid disease was discovered before demonstrable malignant changes had developed (2) The patient's attitude and willingness to co-operate were marvelous When this man was confronted with the facts concerning his disease and the serious nature of it and the very definite risk the radical surgical treatment entailed, he promptly made up his mind that he was ready for treatment and that he was going to get well One could not

FIG 7a



FIG 7b



FIG 7c

FIG 7a —Roentgenogram, Case 2 (J G) Showing large bowel filled with barium. Only a suggestion of polypoid is discernible.
 FIG 7b —Case 2 (J G) Following partial evacuation of barium, polyps become evident in several segments of large bowel.
 FIG 7c —Case 2 (J G) Following inflation of bowel with air presence of multiple polypoidosis is strikingly demonstrated.

ask for a patient in better physical condition and in a better frame of mind
(3) In all four stages of the surgical management, the teamwork of surgeon and anesthetist was most satisfactory

FIG 8

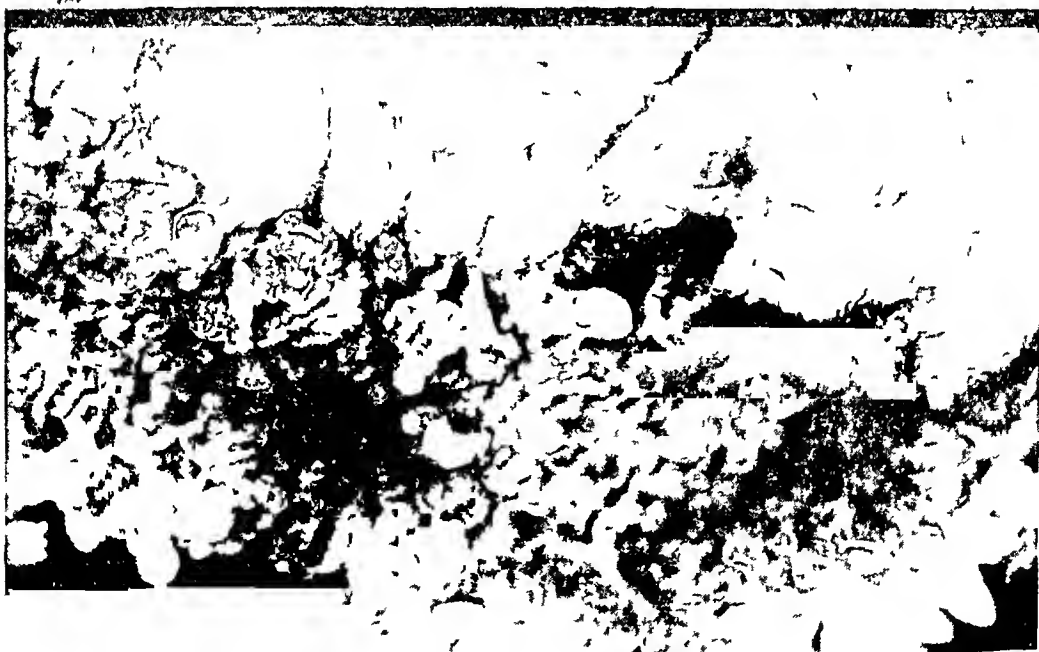


FIG 9

FIG 8—Large bowel, Case 2 (J G), Showing multiple adenomata
FIG 9—Segment of transverse colon, Case 2 (J G), taken under water. Showing countless adenomata

Case 2—J G, age 38, an Apprentice Seaman, was born in Tepeyanez, Mexico. He entered the United States Navy, July 3, 1943, as a Mexican national. He was admitted to the sick list, December 27, 1943, with a "Diagnosis Undetermined (colitis, chronic)." His chief complaints were recurring abdominal pain, occasional vomiting,

POLYPOSIS OF COLON AND RECTUM

and diarrhea at intervals (4-5 stools daily) for five years—stools sometimes contained blood. In 1939, he was examined roentgenologically twice, the second examination was thought to indicate the existence of a stomach ulcer. This, however, was never confirmed. Family history was suggestive of a carcinomatous predisposition. The mother,



FIG 10—Case 2 (J G) Roentgenogram showing functioning ileosigmoidostomy after large bowel had been removed

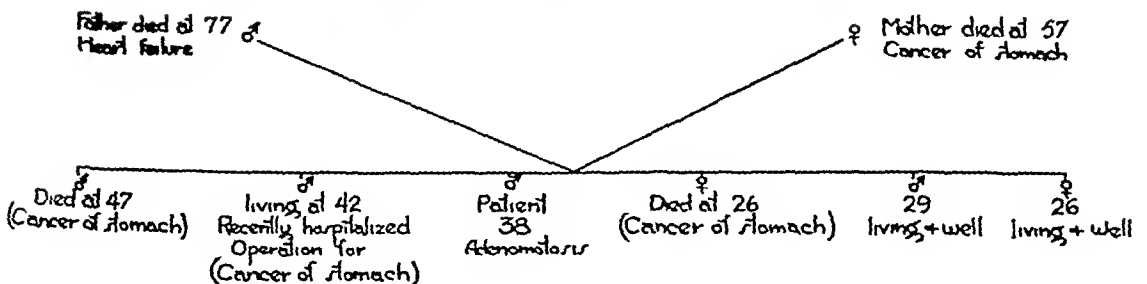


FIG 11—Case 2 (J G) Diagram of family history

one brother and one sister were said to have died of cancer of the stomach. One brother, recently hospitalized, was said to have cancer of the stomach.

Physical examination upon admission revealed a swarthy Mexican of medium stature. Tenderness, with muscle guarding, was elicited in all abdominal quadrants.

Proctoscopic examination revealed internal hemorrhoids, Grade 2, and numerous small sessile polypi, with intervening mucosa of normal appearance. There was no evidence of an ulcerative colitis. Barium enema and roentgenologic study revealed a honeycomb irregularity of the barium contour of the colon throughout its entire extent, but the departure from normal was slightly more prominent in the left half of the large bowel. After evacuation of the barium, air injection of the colon strikingly demonstrated almost complete coverage of the mucosal lining with rounded granulomata or small polypi averaging 3 Mm in diameter. These changes were minimal in the cecum and ascending colon, but from the hepatic flexure to the upper rectum there appeared to be more involved mucosa than uninvolved space between (Fig 7a, b and c). It was interesting to note that in spite of this extensive involvement, there was an average tone to the large bowel, the diameter of which was average in size and normal haustration and mass movements were observed. Irritability and tubular configuration of this bowel, the characteristic signs of colitis, were constantly absent. Gastro-intestinal roentgenology revealed no evidence of cancer in the upper G I tract. The duodenal cap showed a deformity along its lesser curvature side. There was no ulcer crater demonstrable on the lesser curvature. Within four hours the stomach had emptied completely, demonstrating the absence of obstruction. The small bowel appeared to be normal. The findings suggested scarring of the cap as a result of an old healed duodenal ulcer. Oral cholecystograph showed a normally functioning gallbladder and no evidence of stones.

Through the sigmoidoscope all of the adenomatoma from the pectineal line to the pelvic sigmoid were fulgurated and following healing the bowel mucosa was free of evidence of polypoid disease.

On January 1, 1944, under spinal anesthesia and through a suprapubic incision, a side-to-side ileosigmoidostomy was established between the terminal ileum and the pelvic sigmoid (Fig 10). The patient's convalescence following this operation was uneventful. The operative wound healed by first intention, and aside from a diarrhea amounting to from 5 to 10 stools daily which lasted about two weeks, the bowel function returned to normal and the bowel movements were reduced to an average of 2 to 3 daily. The patient was somewhat anemic and received several transfusions during the first three postoperative weeks.

The second part of his operative procedure was planned for the latter part of February, however, an acute tonsillitis with peritonsillar abscess supervened and after the acute process subsided, the patient was transferred to the Eye, Ear, Nose and Throat Service for a tonsillectomy. Tonsillectomy was done on March 29.

On April 20, 1944, under spinal anesthesia through a long left rectus incision, the terminal ileum was divided. The distal end of the ileum was closed and a colectomy which included the entire large bowel from the cecum to the site of the sigmoidal anastomosis with the ileum was performed (Fig 8). The proximal end of the sigmoid was closed. The peritoneum and rectus fascia were closed with interrupted stainless steel wire sutures. Healing of the operative wound was again by first intention, and save for a temporary threat of small bowel obstruction following this operation, the patient's convalescence was uneventful. Bowel function was not interrupted. He was allowed up and about on the tenth postoperative day and within a month the patient was entirely symptom free subjectively and he was having one or two formed stools daily.

Gross examination of the excised colon revealed an 80-cm segment including a stump of ileum, the cecum and appendix with omentum attached to the midsegment of the bowel. The mucous surface was studded with multiple polypi varying in size from pinpoint to 1.5 cm in diameter, some were attached to long pedicles (Figs 8 and 9). At the splenic flexure of this bowel segment, in the mesentery attachment, there was a large area of induration 10 x 5 cm. This was separate from the bowel wall. The mucosa adjacent to this area was not different from the rest. Microscopic examination

revealed no evidence of malignant degeneration in any of the several polypi examined. The above referred to indurated mass showed no evidence of malignancy but consisted rather of fibrous tissue in which there was slight perivascular lymphocytic infiltration.

The patient's family history is diagrammatically illustrated in Figure 11.

CONCLUSIONS

1 Multiple polypoid disease of the colon is an inheritable condition attended by an extreme predisposition to malignant degeneration early in life.

2 The importance of the use of barium enemata and a contrast film following injection of air as a diagnostic measure is emphasized.

3 Radical surgical intervention, namely, total colectomy, is warranted, and carries with it the only hope of permanent cure.

4 Ileosigmoidostomy followed by resection of the intervening segment may be done in lieu of total colectomy in cases where the lesion in the rectum and rectosigmoid can be removed by fulguration.

5 Two case reports are added to the literature. The first is illustrative of one, the second of the other of the surgical procedures referred to.

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PORTAL VEIN THROMBOSIS FOLLOWING REMOVAL OF RUPTURED SPLEEN

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THROMBOSIS of the splenic and portal veins is a not uncommon, though often unrecognized complication following splenectomy^{1, 2}. This operation is occasionally followed by fever, sometimes chills and sweats, vague gastrointestinal symptoms including abdominal pain, nausea, vomiting, and distention which are prolonged and not easily accounted for. It is suggested that in many of these cases some degree of pylethrombosis exists.

Ordinarily the gastro-intestinal symptoms persist for only a short time then clear and the patient recovers. It is possible that readjustments in the portal blood flow made necessary by removal of the spleen, partial thrombosis of the portal vein or its tributaries, or both, may account for the symptoms. The subsequent disappearance of symptoms may be explained on the basis of establishment of collateral circulation or recanalization of the thrombosed vessels.

The literature contains numerous references to the subject of portal vein thrombosis^{3, 5, 6}. In the main, these are concerned with the medical aspects of the problem. The literature on thrombosis following splenectomy has been well summarized by Davis and Sharpe⁷. This complication seems most likely to occur in splenic anemia. In 1895 Delatour⁸ reported a case which demonstrated this complication. Mayo⁹ stated in this regard "Of the ten per cent of patients who died in the hospital following splenectomy the majority died of progressive thrombophlebitis extending from the splenic pedicle into the portal vein."

The studies of Rosenthal,¹⁰ and others,^{11, 12} have indicated the importance of the platelet count in predicting the chances of thrombosis postoperatively in this disease. The thrombocytopenic group seemed to recover without incident, while those in the thrombocythemic group had a high incidence of portal thrombosis.

Davis and Sharpe⁷ reported a case of splenic and portal vein thrombosis following splenectomy for hemolytic jaundice. So far as we are able to determine, this condition has not been reported as a postoperative complication in thrombocytopenic purpura.

Elhason and Stevens¹³ report no deaths from portal thrombosis in a large series of cases subjected to splenectomy for splenic anemia, thrombocytopenic purpura, and ictero-anemia.

Thrombosis of the portal vein has also been reported following traumatic rupture of the spleen in which no operation was performed¹⁴. One gets the impression from various writers that splenic vein and portal vein thrombosis

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is a frequent complication of splenectomy in general. However, so far as we can ascertain no cases have been reported in which this complication followed the removal of a ruptured spleen. We believe the present case represents an instance of portal thrombosis subsequent to removal of a ruptured spleen which, in turn, precipitated an acute cholecystitis on the basis of a previously diseased gallbladder. It seems likely that interference with venous drainage was sufficient to cause edema and infarction of the gallbladder wall and this together with stones led to obstruction of the cystic duct. This conception of the pathogenesis is in agreement with the teachings of the late Edmund Andrews.¹⁵ Death resulted from shock and hemorrhage following cholecystectomy.

Simonds¹⁴ in a comprehensive review of the subject of portal thrombosis, stated "alterations in composition of the blood, slowing of the blood flow and injury to the lining of the vessel have been accepted as the fundamental factors of causation of thrombosis in general since the pioneer but thorough work of Cohnheim and Welch.

The factors predisposing to thrombosis cited by Simonds, which seem to be of importance in the present instance are

(1) Alteration in the composition of the blood. The presence of a marked platelet increase following splenectomy ranging up to about 1,500,000 on the eighth day is demonstrated in the report of Rousselot and Illyne.¹⁶ Thrombocytosis and leukocytosis are said to persist.¹⁷ Other factors to be considered are operative shock, dehydration, and alterations in serum proteins.

(2) Alteration in portal blood flow occurs by virtue of the ligation of the splenic vein. It is estimated that normally about 20 per cent of the portal blood volume is carried by the splenic vein (Burton-Oritz, Mayo). Removal of this supply results in decreased portal flow. One would anticipate thrombosis of the distal portion of the splenic vein. Should the process progress it seems clear that the portal vein may be involved by thrombosis or embolism stemming from the splenic vein.

(3) Alteration in the wall of the splenic vein secondary to operative trauma. This factor may vary according to the technical difficulties involved. There is no doubt that tissue trauma is greater when the spleen is large, adherent, or otherwise difficult to remove. It is to be expected that splenectomy under emergency conditions may be somewhat more traumatic than in the elective operation.

(4) Inflammatory changes in the splenic pedicle or adjacent structures resulting from the initial trauma to the abdomen or from absorption of the tissue of the splenic pedicle, blood clots, etc. In some instances local sepsis may contribute to thrombosis of the splenic vein or portal vein.

(5) Previous diseases of the portal vein such as phlebosclerosis and syphilis may provide sufficient basis for thrombosis when other factors are superimposed.

Case Report—A R., white, male, age 35, a shipyard worker, entered Providence Hospital February 21, 1943. Five hours before admission the patient had fallen across an iron rail striking his left lateral costal margin. He stated that moderately severe pain occurred immediately and he felt "knocked out." Later the pain became generalized, but was especially marked in the left upper quadrant. There was pain on movement or deep inspiration, but no pain referred to the left shoulder. There was no nausea or vomiting.

The past history revealed that the patient had been perfectly well except for an attack of acute abdominal pain which had been diagnosed gallbladder trouble in 1937.

Physical Examination—Temperature, 98° F, blood pressure, 106/60, pulse, 100. The patient was pale and perspiring profusely. Considerable pain was noted on inspiration. Over the left 10th rib in the midaxillary line there was an area of ecchymosis 2.5 cm in diameter. There was no evidence of fracture of the rib. The lung fields were clear. The heart was not enlarged. The tones were somewhat distant, but there were no murmurs. The abdomen was slightly distended and tympanitic to percussion. There was some bulging of the flanks, but neither shifting dullness nor fluid wave could be demonstrated. The extremities were normal. The remainder of the physical examination revealed no changes.

Laboratory Data—Hemoglobin, 93 per cent (12.83 Gm), R B C, 4,290,000, W B C, 14,600. Differential count: P M N 64, staff cells 18, small lymph, 11, monocytes 7, sedimentation rate 1 Mm in 15 min, 8 Mm in 45 min. Urine showed albumin 2 plus, pus cells 2 plus, red cells negative and bacteria 1 plus. The Kahn test was negative.

Examination of the blood three hours after admission revealed that the hemoglobin and red cell count were essentially the same, but that the white blood cell count had risen to 16,500, and the P M N's were reported as 72 and the staff cells 16.

It was our impression that the patient had a ruptured viscus, almost certainly the spleen. The patient was observed for a period of three hours during which time the signs and symptoms did not change appreciably. He continued to have diffuse abdominal pain and tenderness, direct as well as rebound, especially in the lower abdomen. The spleen was not palpable. The pulse rate remained elevated. The blood pressure showed no tendency to fall. Because of failure to improve and the very suggestive picture of intraperitoneal hemorrhage secondary to rupture of the spleen, operation was advised and performed.

Operation—Under closed cyclopropane, oxygen and ether anesthesia, a long left upper rectus incision was made. Many large blood clots together with a large quantity of free blood was encountered, chiefly in the region of the spleen. The spleen was moderately enlarged and two deep lacerations were present over its convex surface. There was active bleeding from this area. The liver appeared normal. The gallbladder was not examined.

The spleen was delivered and its pedicle was doubly clamped and cut. The pedicle was tied with No. 2 chromic catgut transfixion sutures. When complete, the operative field appeared dry and the blood clots were removed. The wound was closed.

The patient received 1000 cc of 5 per cent glucose in normal saline in the operating room, and 400 cc of plasma following the operation. His blood pressure dropped to 84/56 toward the end of the procedure and remained at about this level during the night. The following morning the hemoglobin was 75 per cent (10.35 Gm), and the red cell count 3,540,000. The postoperative course was characterized by frequent nausea with occasional emesis. A considerable degree of paralytic ileus with distention was observed from the second to the fifth postoperative day. The patient had a disturbing cough and expectorated a moderate quantity of thick mucus from time to time, but there was no demonstrable atelectasis or pneumonia. The temperature rose to 101.4° F on the day following operation, and slight daily elevations averaging about one to two degrees above normal were observed until discharge from the hospital on the seventeenth postoperative day.

On the night prior to expected discharge from the hospital the patient complained of steady severe pain in the left upper quadrant together with profuse sweating and weakness. This episode seemed to follow the ingestion of food. The pain was not relieved by changes in position, but gradually disappeared after administration of morphine. The following day the patient felt well and was discharged from the hospital, March 13, 1943, apparently recovered.

While at home the patient had recurring attacks of pain localized to the left upper abdomen. The pains were never cramping in type nor was it associated with nausea or

vomiting. They seemed to occur immediately after eating. There was no disturbance in bowel function, and no significant rise in temperature at this time. There was no abdominal tenderness or distention. Because of persistence of pain the patient was readmitted on March 16, 1943.

Blood Examination—Hemoglobin, 86 per cent (11.87 Gm), R B C, 4,610,000, W B C, 13,350, P M N, 54, S L, 40, staff cells, 6. Sedimentation rate 20 in 15 min, 66 in 45 min.

Roentgenograms of the chest showed slight elevation of the right leaf of the diaphragm, but the lung fields appeared normal, and one of the abdomen showed the entire colon to be filled with gas, but no evidence of small bowel distention.

It was our impression that the patient had a residual collection of pus or blood in the left upper quadrant and conservative treatment was outlined.

The following day the pain had shifted to the right upper quadrant and there was definite tenderness and muscle spasm over the region of the gallbladder. There was no nausea or vomiting. The temperature rose to 101.4° F, and the pulse rose to 128 per minute during the day. The patient continued to complain of pain over the gallbladder area, and careful investigation of his past history revealed that a similar episode had occurred in 1937 at which time the diagnosis of gallbladder disease had been made. On March 22 slight jaundice was present. The icterus index was 22. Under conservative measures the patient gradually improved. The pain and tenderness subsided and the jaundice disappeared.

On March 29, the blood examination showed W B C, 8,600, P M N, 63, P M E, 3, S L, 22, mono, 6, staff, 6. Sedimentation rate 32 in 15 min, 100 in 45 min. The icterus index was 10.

The patient's general condition appeared good. He was prepared for operation by the administration of a high carbohydrate, high protein, and low fat diet as well as vitamin K and bile salts. On March 31, 12 days after onset of acute right upper quadrant pain, operation was undertaken for subsiding acute cholecystitis, with probable cholelithiasis and choledocholithiasis. The patient appeared to be a satisfactory surgical risk, however, it was later learned that he had repeatedly stated to others that he would not survive operation.

Operation—March 31, 1943—Anesthesia cyclopropane, oxygen and ether. When the abdomen was opened through a right upper rectus incision, the gallbladder was found to be entirely walled-off by dense adhesions between omentum and the duodenum. The adhesions were extremely vascular and bled freely on slight trauma. The gallbladder was tense, dilated, and friable. It appeared markedly inflamed and contained a number of gallstones. The structures about the porta hepatis were, likewise, edematous and friable. The cystic duct contained impacted stones. The common bile duct felt normal to palpation. Because of subsequent events, adequate exploration of the common duct was not carried out.

Following freeing of adhesions between the gallbladder and the surrounding structures and the exposure of the common duct, profuse hemorrhage was encountered. This appeared to be venous in type. Attempts to control the bleeding by compression of the structures of the porta hepatis and ligation and application of hot wet packs were unsuccessful. The tissues were so friable that clamps or ligatures would not hold and each manipulation resulted in increased bleeding. It seemed that the hemorrhage came from one of the tributaries of the portal vein. During the period when packing was in place the gallbladder was removed from the fundus down to the cystic duct. The cystic vessels and the cystic duct were separately cut, clamped and ligated. The patient received plasma transfusion during the procedure and was also given caffeine. Upon completion of the procedure his condition was poor and a gauze pack was left in the bleeding area and brought out the upper end of the wound.

The patient failed progressively, in spite of blood and plasma transfusions, and

expired four hours later. The clinical cause of death appeared to be operative hemorrhage and shock.

Pathologic Examination—Surgical Specimens (Dr T. D. Robertson) *Spleen* (Fig. 1). The spleen weighs 340 Gm. Two tears are present on the diaphragmatic surface of the spleen. The first measures 11 cm. in length, and the second is a V-shaped tear measuring 7 cm. A third tear is present on the left margin and measures 5 cm. *Pathologic Diagnosis*: Multiple traumatic rupture of the spleen, with hemorrhage.



FIG. 1.—Drawing of spleen showing lacerations containing some clotted blood.

Gallbladder. The gallbladder is a rigid, thick-walled structure 9 cm. in length and 3 cm. in diameter. The serosal surface is hemorrhagic and covered with a fibrin coating. The wall shows hemorrhagic mottling, fibrosis, and reaches a maximum thickness of 1.0 cm. There is bile-staining of the mucosa and yellow cholesterol streaking. It contains several cholesterol stones. Microscopic examination shows the wall to be thick and the site of extensive hemorrhage. There is some coagulation of the mucosal surface associated with the diffuse hemorrhage. There is infiltration by pus cells, eosinophils, and lymphocytes. Near one area of deep ulceration a number of foreign

body giant cells are seen *Pathologic Diagnosis* Marked hemorrhagic acute exacerbation of a chronic cholecystitis, with cholelithiasis

Postmortem Examination (Dr T D Robertson) The only significant changes are found in the abdomen. Approximately 300 cc of bloody fluid is present in the right upper abdomen. Careful search for the bleeding point failed to reveal it. The tissues in the region of the common duct are indurated. The common duct is dilated and near the ampulla there are eight small mulberry cholesterol stones none more than 4 Mm in diameter. The hepatic artery is then followed throughout and shows no bleeding point. The ligatures on the cystic artery and duct are intact. The portal vein (Fig 2) is found after dissecting through edematous fibrous tissue, and it is noted

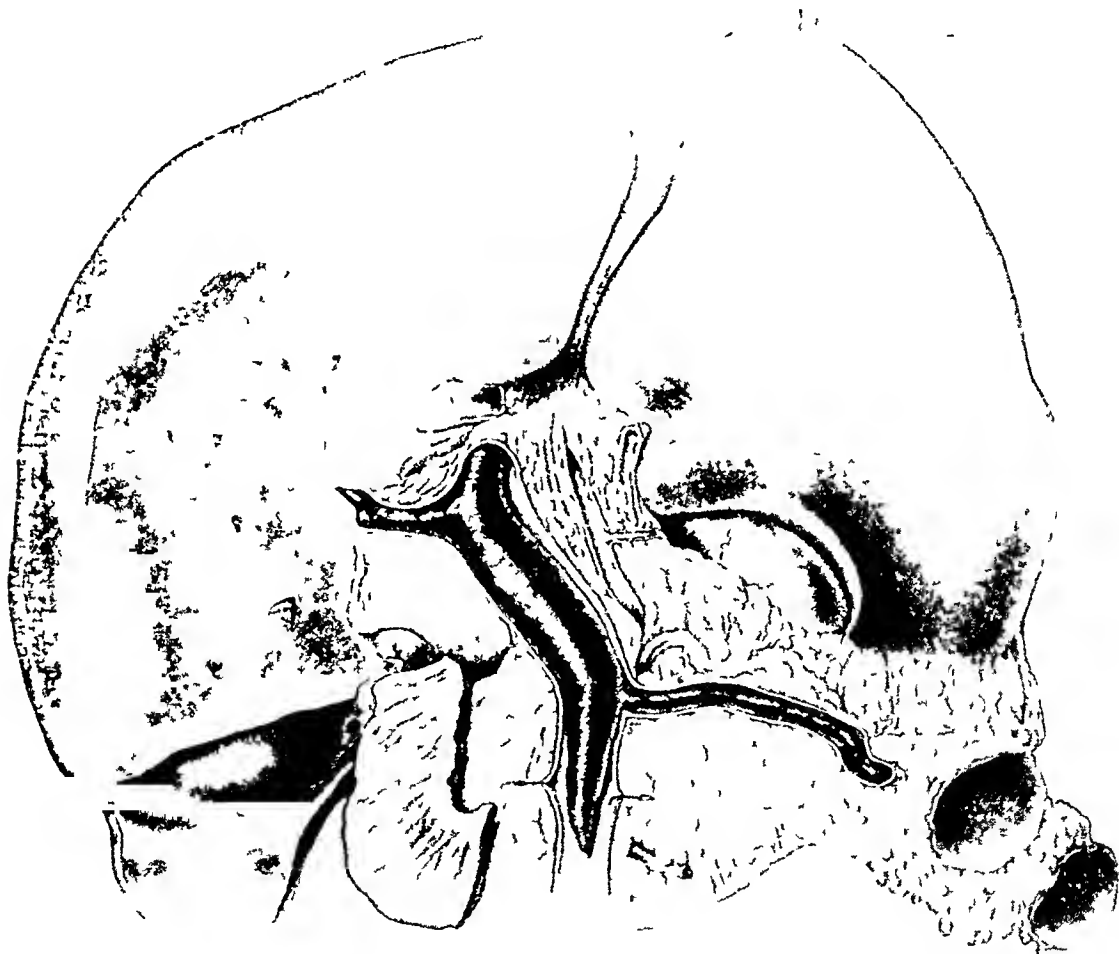


FIG 2—Drawing of liver, pancreas, duodenum, accessory spleen and portal vein and its tributaries. Note extent of thrombosis. The gallbladder had been removed at operation.

that it is filled with an adherent, rather mushy, red blood clot which is definitely a thrombus. It extends into the right and left branches as a firm, adherent, pink clot. The right lobe of the liver is much softer than the left, indicating probably more blood was cut off in the right lobe than in the left. This clot extends in a polypoid manner for a distance of 6 cm into the upper portion of the superior mesenteric vein. The splenic vein is small, contracted, 8 Mm in diameter, and filled by red to brown clot. The splenic artery is found at its distal portion to be tortuous and filled by dark red clots for a distance of about 2 cm. There is an accessory spleen measuring 3 cm in diameter. The pancreas is somewhat edematous. The liver is enlarged and appears fatty. The right lobe is friable and shows diffuse red stippling. The splenic bed is

filled by adhesions. There are no blood clots found. The small intestine and colon appeared unchanged. The adrenal glands and other abdominal organs show no changes.

Microscopic Examination—Pancreas Except for postmortem autolysis the pancreas is not unusual. *Liver* The central lobular hepatic cells are undergoing disintegration with pyknosis of nuclei and fragmentation. A slight increase in pus cells in some areas is noted. The sinusoids contain very little blood. Central lobular hepatic cells also contain large and small fat droplets. *Small Intestine* There is no edema or other change. *Lung* There is slight engorgement of the vessels. *Kidney, adrenal glands, myocardium* No changes.

Pathologic Diagnosis Death due to postoperative shock following cholecystectomy. Probably contributing much to this was liver deficiency on the basis of portal vein thrombosis. This was built up from a thrombus of the splenic vein, which probably followed previous splenectomy for traumatic rupture of the spleen.

Histologic examination of various levels of the portal system, the representative areas from which photomicrographs were made, are indicated in Figure 3.

The splenic vein (Fig 4) is occluded by a fresh thrombus, which only in focal areas shows early softening and attachment to the vessel wall. This section apparently represents an area some distance from the point of ligation of the splenic vein.

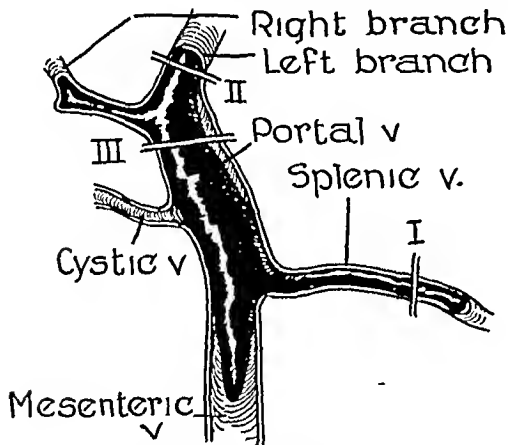


FIG 3—Areas from which photomicrographs were made

The section through the left branch of the portal vein presents the picture of a truly organized thrombus. Here capillaries and fibroblastic proliferation constitute the predominant features of this also occlusive thrombus. Attachment to the wall of the vessel as well as beginning canalization has occurred (Fig 5).

Section through the upper portion of the portal vein (Fig 6) shows an occlusive thrombus of an age between the clot in the splenic vein and the organized thrombus in the left branch of the portal. A large area of central softening is noted as well as beginning organization of the circumferential attachment to the vessel wall.

Other sections taken from the more peripheral portion of the portal vein reveal fresher thrombus formation, apparently the result of propagation of the thrombus from above downward. Likewise, in that section taken through the right main branch of the portal system, a thrombus of earlier age than that in the left is noted.

COMMENT—Following surgical ligation of the splenic vein the thrombus formed at this point must have been, in part, dislodged. This portion of thrombus, now circulating in the portal system, lodged in the left main branch of the portal vein producing an occlusion. The secondary attachment and the resultant organization of this thrombus then constituted a thrombus head from which retrograde propagation occurred. This propagating clot finally encroached upon the ostium of the cystic vein with obstruction to the venous return from the gallbladder. The resulting vascular stasis in this organ produced the clinical picture of acute cholecystitis.

DISCUSSION—From the histologic studies in this case, it may be concluded that portal thrombosis occurred as a direct result of splenectomy. It must be borne in mind, however, that previous disease of the biliary tract may have

been a contributing factor. There is no evidence that direct or indirect trauma was of importance since the blow received was relatively slight, well-localized and away from the upper abdomen.

The clinical course should have suggested this complication had not biliary tract disease been superimposed. Pallette⁵ has pointed out that the symptoms resulting from portal thrombosis usually appear as sudden, acute upper abdominal pain which may appear in the right upper quadrant and simulate gallstone colic. In chronic thrombosis Simonds⁶ notes that there may be no relationship to the taking of food. In the present instance eating usually precipitated the pain, which was at first located in the left upper abdomen. We believe, therefore, that the inadequacy of the portal system to



FIG. 4.—Fresh thrombus in splenic vein (A). Artery (B). (Low power). Note prominence of corallike lamellae of congealed platelets, absence of organization indicating freshness of the thrombus.

meet the increased circulatory demands of digestion was sufficient to cause pain.

The presence of intermittent fever, leukocytosis, and increased sedimentation rate was evidence of serious intra-abdominal pathologic changes. In a case not complicated by biliary tract disease, it would seem that thrombophlebitis of the portal vein should be considered second only to an intra-peritoneal abscess.

Intestinal dysfunction is dependent upon the degree of interference with the mesenteric veins. In this case there was little or no obstruction, but in Delatour's⁸ classical case the symptoms were those of acute intestinal obstruction because of the cutting off of a large part of the circulation.

Bassler¹⁸ has found that roentgenologic studies of the small intestine show marked slowing of the transit function from the jejunum down to the transverse colon in portal thrombosis. This again is dependent upon the degree of interference with the mesenteric venous flow, and it is unlikely that significant changes could have been demonstrated in this case. It is inter-

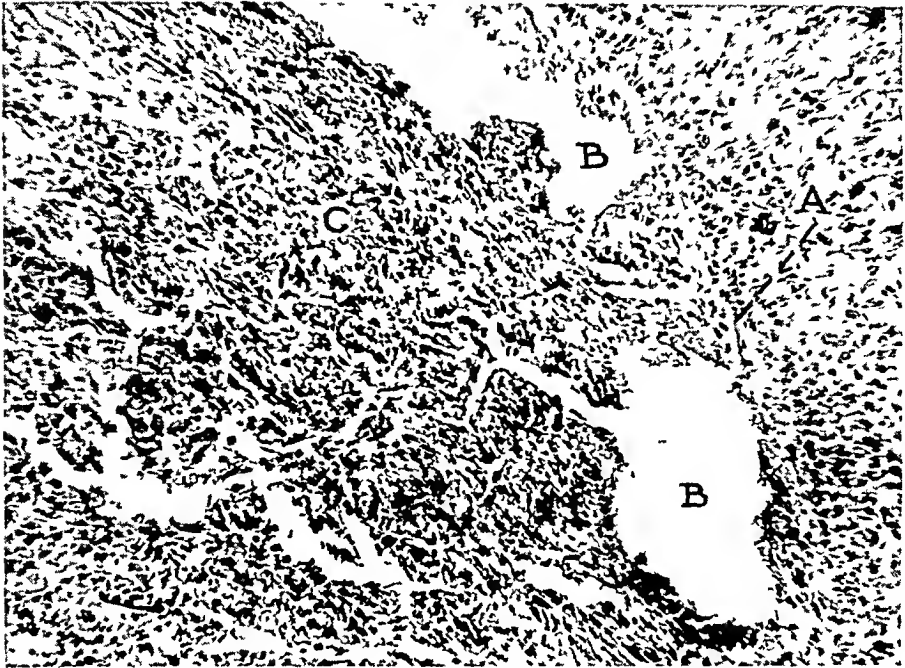


FIG 5—Organized thrombus in left branch of portal vein (High power)
A Intimal surface of vessel B Canalization C Organized thrombus
Section showing organized occlusive thrombus and beginning canalization

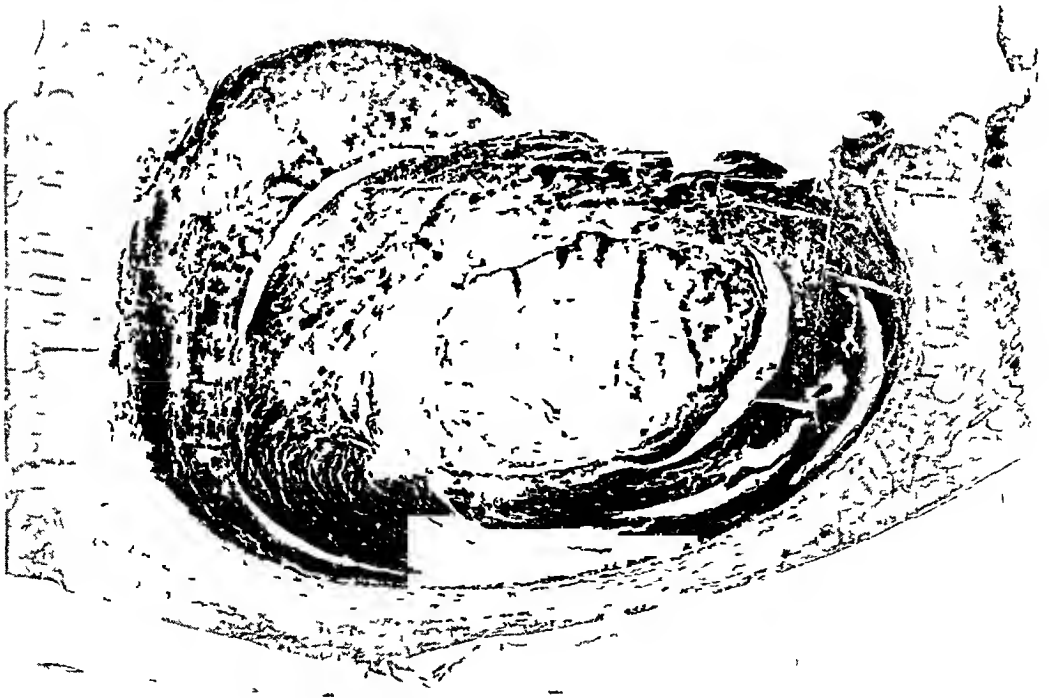


FIG 6—Organizing thrombus in upper portal vein (Low power)
Note peripheral attachment with beginning organization of thrombus

esting to note the degree of gaseous distention of the colon which was present in our case. It is suggested that portal blood flow may have been decreased sufficiently to cause diminished absorption of gas from the bowel.

Regarding the pathogenesis of an acute exacerbation of chronic cholecystitis in this patient, there seems to be no question about the rôle of vascular impairment. At operation, it was obvious that the venous pressure in the portal system greatly exceeded the normal. This back pressure through the cystic vein would seem to have been sufficient to lead to edema, infarction, hemorrhage and ulceration of the gallbladder wall.

At this time it seems pertinent to remark that cholecystectomy should have been delayed for a much longer period. It is probably a good rule to delay all elective intraoperative operative procedures following splenectomy until adequate circulatory readjustments have been made. How long this might be is difficult to estimate. It is also to be recalled that reaction to shock and hemorrhage shortly following splenectomy may be decreased since the spleen is said to be an important organ of homeostasis.

Murray and MacKenzie¹⁹ demonstrated clinically, and experimentally in dogs that heparin can be of great value in preventing thrombosis of the portal vein following splenectomy and bowel resection for mesenteric thrombosis. This work suggests the possibilities of the anticoagulant drugs in the postoperative care of cases where this complication may be expected or suspected. This is particularly true for splenic anemia.

We were interested in the rôle the mental attitude of the patient played in the ultimate outcome. It has been repeatedly emphasized that patients who firmly believe they will not survive operation, frequently do not. Upon this basis most surgeons rightly will refuse to undertake operation. In this case, had we known of the patient's feelings in the matter it is likely that we too would have delayed. It is possible that had the patient not succumbed, recanalization and establishment of collateral circulation of sufficient degree to maintain good or fair health would have occurred.

CONCLUSIONS

1. A case of clinically unrecognized splenic and portal vein thrombosis following splenectomy for traumatically ruptured spleen is reported in detail.

2. In this case, acute cholecystitis on the basis of a previously diseased gallbladder is believed to have been precipitated by portal thrombosis which caused vascular changes in the gallbladder wall.

3. Death was caused by uncontrollable hemorrhage and shock during cholecystectomy. The increased portal venous pressure and friability of tissues made complete hemostasis unobtainable.

4. It is suggested that splenic and portal vein thrombosis following splenectomy may be a frequently unrecognized complication. Prolonged fever, abdominal pain sometimes related to food intake, abdominal distention, increased leukocyte count, and increased platelets and erythrocyte sedimentation rate following splenectomy should suggest to the surgeon the possibility of this complication.

5 Major elective abdominal operations should not be undertaken shortly following splenectomy if the possibility of portal thrombosis exists

6 The anticoagulant drugs, heparin and dicoumarin, may be of value in preventing the onset or extension of thrombosis of the portal vein

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ROENTGENOLOGIC EXAMINATION OF THE ABDOMEN AS AN AID IN THE EARLY DIAGNOSIS OF SPLENIC INJURY

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DAMAGE TO THE SPLEEN is probably the most common serious intra-abdominal injury resulting from blunt force. Clinically three types of bleeding may occur: (1) Extensive rupture with immediate massive hemorrhage, (2) small lacerations which ooze blood slowly over a period of hours or possibly days, and (3) delayed splenic rupture. These types of splenic damage have been discussed by many authors. By delayed splenic rupture is meant severe secondary hemorrhage occurring from the spleen days, weeks or even months following the original injury. This type of bleeding occurs in about 14 per cent of all splenic injuries.¹⁰

In the first type of injury to the spleen the diagnosis is usually easily made and splenectomy carried out. The second and third types of splenic injuries are difficult to diagnose in the hours immediately following trauma, especially in the presence of associated injuries. The patient's symptoms and signs may disappear completely or so improve that he may be allowed to resume full activity. Then after a latent period of hours, days, or even months secondary hemorrhage may occur, usually of such severity that circulatory failure ensues rapidly.

The time to remove a slowly bleeding spleen is early, before blood loss threatens life, and the ideal method of handling a delayed rupture of the spleen is to perform splenectomy early in the latent period. Diagnosis must, therefore, come early, and yet the difficulties of such early diagnosis are great. Clinical symptoms and signs may be equivocal, and the accessory examinations which the clinician has heretofore used may be dangerous, time-consuming, inconclusive, or all three.

Hematologic work may or may not aid. Abdominal aspiration or peritoneoscopy have been advocated, but these examinations are more difficult and more dangerous than the taking of a plain film of the abdomen. There is evidence that the roentgenologic examination of the abdomen can be of great aid in establishing early the diagnosis of a lacerated spleen.

Various authors have described roentgenographic aids in the diagnosis of lacerated spleen. Webb⁹ reported increased density in the left upper abdominal quadrant, with elevation of the left side of the diaphragm, displacement of the stomach to the right, and free fluid between loops of intestine. Zabinski and Harkins¹⁰ mention elevation of the diaphragm in one patient and medial displacement of the colon in another. They also mention Bancroft's experience in administering barium sulfate to a boy placing him in the Trendelenburg position, and observing a mass in the region of the spleen displacing the

stomach J M Deaver³ mentions elevation and tenting of the left diaphragm in a patient with a delayed splenic rupture coming on 23 days after injury Burke and Madigan² gave thorium dioxide to a patient with lacerations of spleen and liver and were able to outline the damage in each viscus These roentgenologic procedures are helpful to a limited degree only They are all either signs of advanced hemorrhage, as when visceral displacement is shown, or they are time-consuming, as is thorium, or they are undesirable for other reasons, such as the administration of barium orally

The roentgenographic findings described by Solis-Cohen and Levine^{5,7} may answer the need for a reliable, simple means which will aid in the early diagnosis of minimal to moderately severe splenic damage These authors, in making roentgenologic examinations of the abdomen in three patients suspected of having splenic injury, described obliteration of the splenic shadow, and a dilated stomach, with serration of the greater curvature In each case the diagnosis was confirmed at celiotomy In plain films of the abdomen taken of 100 patients with no demonstrable splenomegaly, the authors did not encounter these findings

Various questions arise concerning these roentgenographic signs (1) Does splenic laceration always cause them? (2) Are the signs dependent upon the size of the splenic laceration or the amount of hemorrhage? (3) Do they occur in damage to viscera other than spleen? (4) Are they present when the spleen plus some other viscus is damaged? (5) Why do these signs occur? (6) Are they present after splenectomy?

During the past few months on the Surgical and Urologic Services of the North Carolina Baptist Hospital and Forsyth County Hospital, three patients with nonpenetrating trauma to the left upper quadrant, left flank and left lower thorax have been studied⁸ A survey of the records of these patients tends to corroborate the findings of Solis-Cohen and Levine,⁷ and lends evidence to help answer the above queries

CASE REPORTS

Case 1—NCB No 25507 (From the Service of Dr H H Bradshaw) M N, white, female, age 13, was admitted at 3 30 P M, February 14, 1944, with a history that at 3 00 P M she had been struck and knocked down by a school bus She was unconscious for 15 minutes, and when seen in the Emergency Room she had amnesia covering the previous 24 hours, although her memory for prior events was good She complained of pain over the left lower chest and in the left upper abdominal quadrant Blood pressure 124/72, pulse 100 to 110 Her occipital scalp was lacerated The chest was clear and there was moderately severe left upper abdominal tenderness There was suggestive increase in the area of splenic dullness No flank rigidity was found, and peristalsis was quiet

Accessory clinical findings were not remarkable save for a leukocyte count of 14,900, with a normal differential Urinalysis revealed 40 to 50 white blood cells and 10 to 20 epithelial cells (h p f), with one plus albumin, and a negative benzidine test

A plain film of the lower chest and abdomen revealed fractures of the left seventh and eighth ribs posteriorly, without displacement The kidney and psoas outlines were

* These patients were operated upon by members of the Resident Staff in Surgery, Doctors Felda Hightower, M C Bowman, and W L Molneux

DIAGNOSIS OF SPLENIC INJURY

normal The splenic shadow was not visualized, the stomach was displaced downward, and there was an unusual amount of gas in the stomach, with serrations of the greater curvature in the cardiac and midportions (Fig 1)

She was observed several hours, with no change in the symptoms or signs Celiotomy was performed at 8 20 P M, February 14, 1944, under cyclopropane, oxygen, and ether anesthesia, using a curved left subcostal incision Ecchymosis was present in all visible parts of the omentum, and 400 cc of dark, liquid blood was found in the peritoneal cavity On the concave surface of the spleen there was an irregular laceration six centimeters

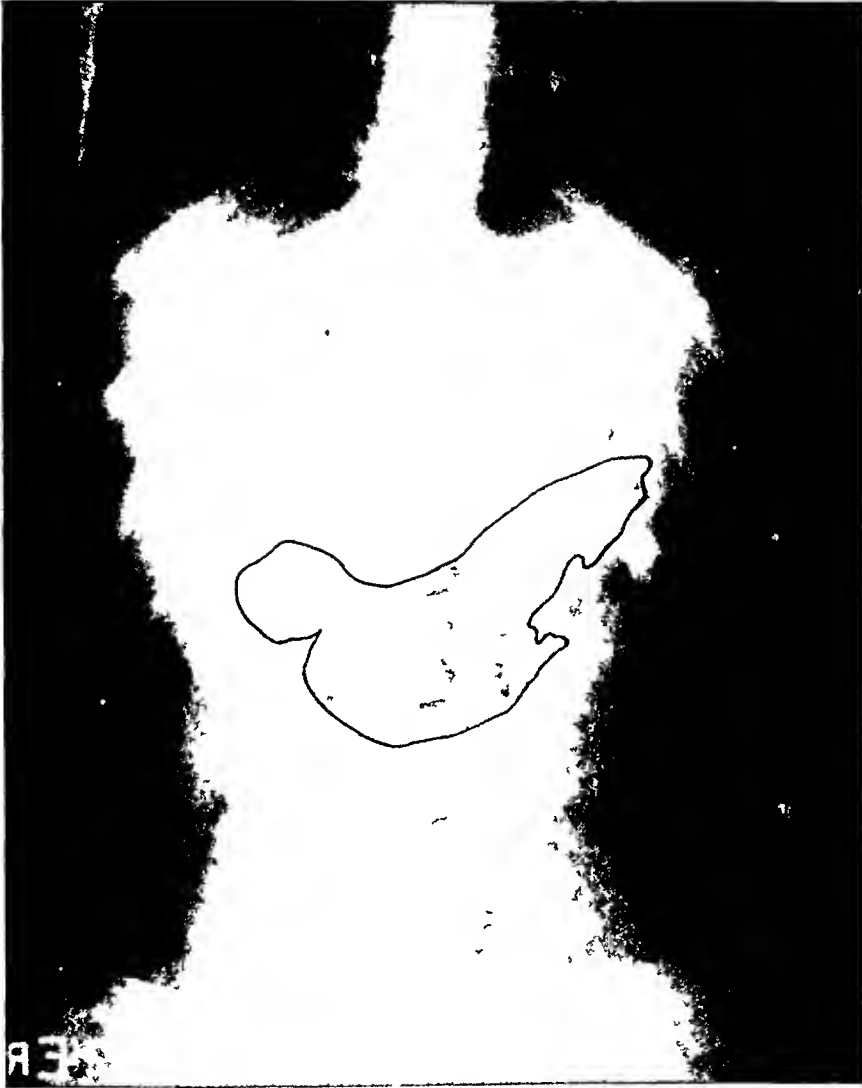


FIG 1—Preoperative plain film of abdomen of Case 1, showing the left diaphragm and stomach outlined with India ink Note downward displacement of gas filled stomach and serrated greater curvature

long, showing at its upper part, excavation into the splenic pulp Postoperatively, the patient received 500 cc of pooled plasma and 500 cc of citrated blood Her course was uneventful, she was discharged on the tenth postoperative day, and she has remained well since

Films of her abdomen made postoperatively showed kidneys and stomach normal in outline, and position (Fig 2)

Case 2—FCH No 2847 (From the Service of H H Bradshaw) O S N, white, male, age 34, was admitted at 12 15 P M April 24, 1944, with a history that two hours earlier he had fallen from a barn, a distance of eight feet, and landed on his left side, striking his left flank Following this he vomited once and had pain in his

left upper quadrant radiating down to his left lower quadrant and genitalia. The pain in his left upper quadrant increased and he noted pain in his left flank.

At the time of admission his temperature was 100° F, pulse 88, blood pressure 130/78. Chest examination was negative. There was muscular rigidity of the left upper and left lower abdominal wall, with tenderness in the left upper abdominal quadrant. In the left flank and over the left lower ribs, there was a diffuse erythematous area, quite tender on even light palpation.

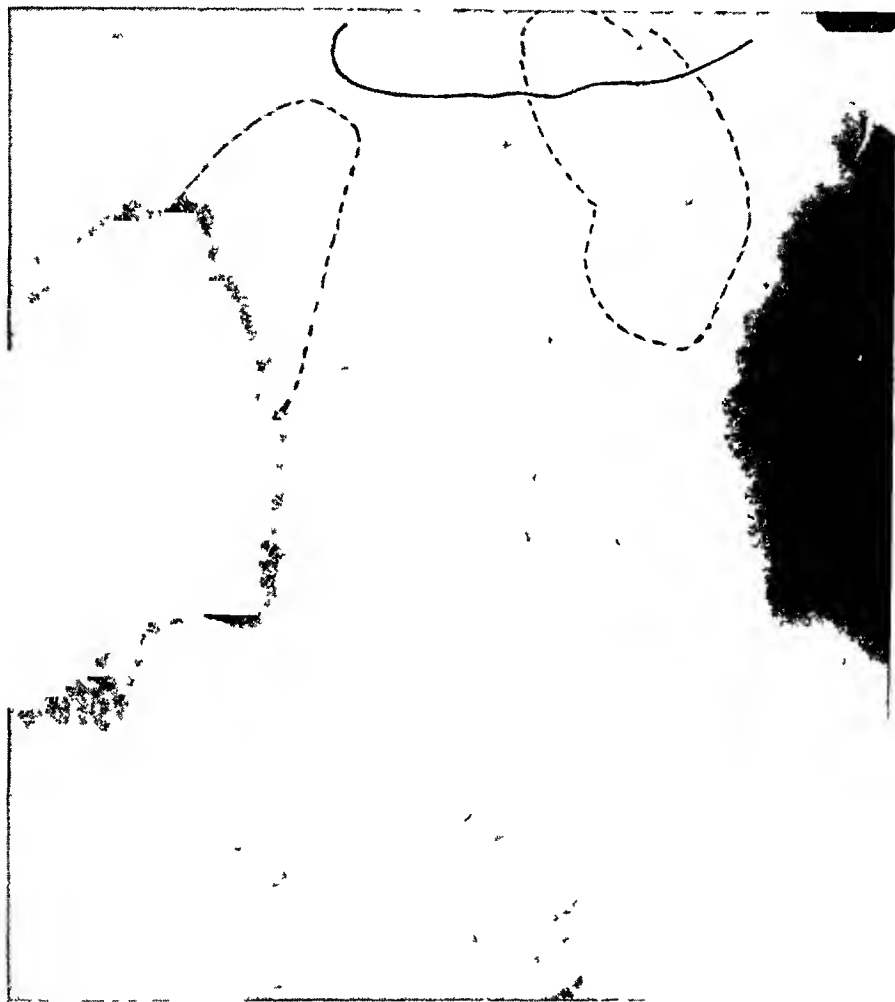


FIG 2—Postoperative film of abdomen of Case 1, showing the greater curvature of stomach and kidney shadows outlined with India ink. Film does not include diaphragm. Stomach is normal in position and greater curvature is smooth.

Accessory clinical findings showed four to six red blood cells and an occasional white cell (hpf) in a voided urine specimen. Otherwise the findings were normal. A plain film of the abdomen showed moderate enlargement of the splenic shadow. The stomach contained much gas, the fundus was displaced downward, and the greater curvature was serrated (Fig 3). The left kidney and psoas shadows were indistinct.

Celiotomy was performed three hours after admission, under cyclopropane, ether, and oxygen anesthesia. There was a small amount of ecchymosis in the mesentery of the splenic flexure. A laceration, 2 cm long, was present on the concave surface of the spleen and blood was slowly oozing from it. There was less than 50 cc of free intraperitoneal blood present. Ecchymosis in the left retroperitoneal tissues gave one the impression of slight bleeding in the left perirenal area. No other evidence of injury

was found Splenectomy was performed, and the patient made an uneventful recovery The hematuria ceased after the first day

Postoperative roentgenologic studies showed gas present in the stomach, with a smooth greater curvature (Fig 4) Excretory urograms showed a normal urinary tract

Case 3—N C B No 28421 (From the Service of Dr Fred K Garvey) E M C, white, female, age 11, was admitted at 4 15 P M, May 22, 1944, with a history that



FIG 3—Preoperative film of abdomen of Case 2, showing the gas in stomach, serrated greater curvature and enlarged splenic shadow

she had been kicked in the left flank by a mule four hours earlier She had fainted several times before being brought to the hospital When examined in the Emergency Room her temperature was 97 8° F per rectum, pulse 160, blood pressure 50/0 There was splinting of the left diaphragm, with definite respiratory lag on the left Examination of the thorax was negative Her abdomen was moderately distended, and acutely tender, but not rigid over the left side There was a large elevated and contused area in the left costovertebral angle, and this area was exquisitely tender The urinary bladder could be percussed three fingers breadth above the symphysis pubis The patient voided 400 cc of grossly bloody urine, which clotted in four minutes

Accessory clinical findings showed a hemoglobin of 9 5 Gm, red cells 4,200,000, white cells 16,800

A plain film of the abdomen showed marked gaseous distention of the stomach, with very little gas in the small or large bowel. The right kidney and psoas shadows were normal. The left kidney shadow was obliterated, and the left psoas shadow obscured by an increased soft-tissue density in this region (Fig 5). An intravenous urogram showed normal excretory function on the right, with complete absence of function of the left kidney (Fig 6).



FIG 4—Postoperative film of abdomen of Case 2, showing stomach normal in position, with much gas in it, but a smooth greater curvature

The patient received blood and plasma and an exploratory celiotomy was performed through a left flank incision. The left kidney was found to be shattered into four pieces, with much clot under tension within Gerota's fascia, and a partial tear of the renal artery and vein. Nephrectomy was performed. The diaphragm was normal, and the tissues adjacent to the posterior surface of the left colon were edematous. The peritoneal cavity was opened and found free of blood, with a normal spleen and normal bowel. The patient was in moderately severe circulatory failure on the table and at the conclusion of the procedure her blood pressure was 90/60. Her postoperative course was uneventful, and she was discharged on her twelfth postoperative day. Plain films of the abdomen, made postoperatively, revealed her stomach normal in position and containing a small amount of gas. The small part of the greater curvature that could be visualized was smooth.

In these three patients, one had a lacerated spleen and two fractured ribs, with no evidence of any other lesion, and her plain film demonstrated very clearly the signs described by Solis-Cohen and Levine. The second patient with laceration of the spleen as well as damage to the left kidney also had the characteristic roentgenographic findings. The third patient with a shattered kidney and a normal spleen, had much gas in the stomach



FIG 5 —Preoperative film of abdomen of Case 3, showing marked gaseous distention of the stomach with smooth greater curvature. Right psoas shadow is normal, left psoas shadow is obliterated.

but a smooth greater curvature, along with obliteration of the left kidney shadow, and an obscure left psoas shadow.

These facts stand as evidence that the gas-containing stomach, with the serrated greater curvature, will show on a plain film of the abdomen when the splenic laceration is small or moderately large, that these findings still occur when some other viscus in addition to the spleen is injured, that these signs are absent when the kidney is ruptured in the presence of a normal spleen, and that they are not present following splenectomy.

The cause of these roentgenographic findings is not clear. A notched, indented or slightly serrated greater curvature may appear occasionally in a plain abdominal film of a patient who has not been subjected to any trauma. Some of these shadows are due to extrinsic masses pressing on the stomach, and some of them are of unknown etiology. Obviously, in such instances the differential diagnosis will rest on the absence of any history of injury or the finding of some extragastric mass. Solis-Cohen and Levine feel that,



FIG. 6—Preoperative excretory urogram of Case 3. Stomach appears the same as in Figure 5. Note absence of excretion of dye by the left kidney.

in a patient who has a lacerated spleen, the gravitation of blood along the gastrosplenic ligament adjacent to the greater curvature is the cause of the serrations seen in the stomach shadow. This could explain the findings in Case 1, but it does not explain them in Case 2, where there was not enough hemorrhage to infiltrate the gastrosplenic ligament.

In Cases 1 and 2 with minimal to moderately severe splenic injury and equivocal clinical findings, the plain films raised strong suspicions that the spleen was lacerated. Once such a suspicion exists, celiotomy is indicated, unless both surgeon and patient are willing to tolerate the anxiety, as well as the danger, that a delayed rupture may occur.

Further experience with these roentgenographic findings in the presence

of damaged spleens is necessary. These patients are offered as evidence to corroborate the findings of Solis-Cohen and Levine, and to stress the importance of plain films of the abdomen and chest when splenic damage is suspected, not alone to help evaluate the injury to the spleen, but to help rule in or out associated thoracic injuries.

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SULFONAMIDE THERAPY IN CLEAN THORACOPLASTY CASES

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THE EMPLOYMENT of the sulfonamides in clean operative cases to prevent wound infections has not been completely successful. Most of the publications regarding the procedure state that some infections have occurred despite the prophylactic use of the drugs. If the sulfonamides have not prevented infections in clean wounds, then of what value is their routine prophylactic employment?

The experience of the Tuberculosis Service at Bellevue Hospital, with the use of the sulfonamides in clean thoracoplasty operations, merits publication. Our report concerns 83 patients who had 203 clean thoracoplasty operations, of which 167 were for parenchymal disease and 36 were for mixed empyemas with bronchopleural fistulae. All of the thoracoplasty operations in the series were clean even though some of the operative procedures in the empyema group approached an infected area. The modern thoracoplasty operation, averaging three ribs a stage, was performed in almost every case, and, generally, silk ligature and suture materials were used throughout. The authors assisted, or performed, most of the operations and observed the patients' convalescence, while the selection of cases for local, oral and nonsulfonamide therapy was determined by the surgical attending staff.

The thoracoplasty cases were grouped into three series: those which had the sulfonamides applied locally, those which received the sulfonamides orally, and the controls in which no sulfonamides were used. In this manner the groups may be compared and contrasted from the data presented. The scope of our investigation includes the patients' local and systemic reactions to the sulfonamides, the blood and wound fluid sulfonamide concentrations when the drugs were employed locally and perorally, and the incidence of contaminations and infections in the clean operative wounds of the different groups.

The first series consisted of 97 cases in which the sulfonamides were applied locally to the thoracoplasty wounds. The sulfonamides were prepared and sterilized in two-, four- and six-gram amounts, with an average of 4.7 Gm. being used per operation. In each, the drug was dusted evenly, without lumping, over the wound surface including the subcutaneous tissues.

No known toxic reactions occurred in any of the cases and there was no evidence of poor or delayed wound healing. Twenty cases of the series of 97 were reviewed to determine the volume of excess wound fluid which was

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aspirated. All 20 cases formed excess wound serum, and the average amount aspirated per case was 328 cc.

The second series of thoracoplasty cases numbered 39, and they received the sulfonamides orally in divided doses for three or four days after the operation. One patient developed jaundice and anemia, which disappeared after the drug was withdrawn and three other patients had hematuria and urinary sulfonamide concretions, but no appreciable oliguria. All wounds appeared healed at the tenth postoperative day. Six of the ten cases analyzed for excess wound fluid had excess fluid and about 135 cc were aspirated in each of the six cases.

The third series was composed of 67 thoracoplasty cases in which no sulfonamides were used, and they acted as the control group. There were no reactions resembling sulfonamide toxicity and all wounds healed promptly. Fifteen cases of the group were examined for excess wound serum and the eight cases which developed excess serum averaged 110 cc.

The three series revealed that the systemic reactions to the sulfonamides occurred only in the group which received the drug perorally, especially in large amounts. No evidence of nonhealing, or even any delay of wound healing, was observed in any case. Excess wound serum exudation occurred in each series, but it was seen more often and of greater volumes in the series of cases which had a sulfonamide applied locally in the thoracoplasty wound.

The wound fluid was aspirated, usually between the second and the fifth postoperative days, from the subscapular space, which was enlarged as a result of the operative procedure. Wound serum sulfonamide concentrations were determined in many of the thoracoplasty cases in which the drugs were applied locally, and the concentrations were so surprisingly low that an investigation of the comparative concentrations in blood and wound fluid was undertaken. Thereafter, sulfonamide levels were determined on each specimen of aspirated wound fluid, while blood samples were drawn at eight, 24 and 48 hours postoperatively. The completed data on 25 thoracoplasty cases in which the sulfonamides were implanted locally were reviewed and the average of the blood and wound serum concentrations are shown in Chart I.

It was assumed from the trend of averages that the peak of the blood sulfanilamide levels occurred before the eight hour specimens were drawn, while the blood sulfadiazine concentrations peaked between the eight- and 24-hour specimens. Likewise, it was assumed that the wound serum sulfonamide concentrations were undoubtedly high immediately after the operation, but they rapidly declined approximating one milligram for each gram of drug applied locally at 24 hours and being insignificant after the fourth day.

We felt that six to eight milligrams of sulfonamide in each 100 cc of fluid was necessary for the optimal therapeutic effect, if wound infections were to be prevented. We sought to secure these higher concentrations of the sulfonamides by returning to the systemic administration, as that method

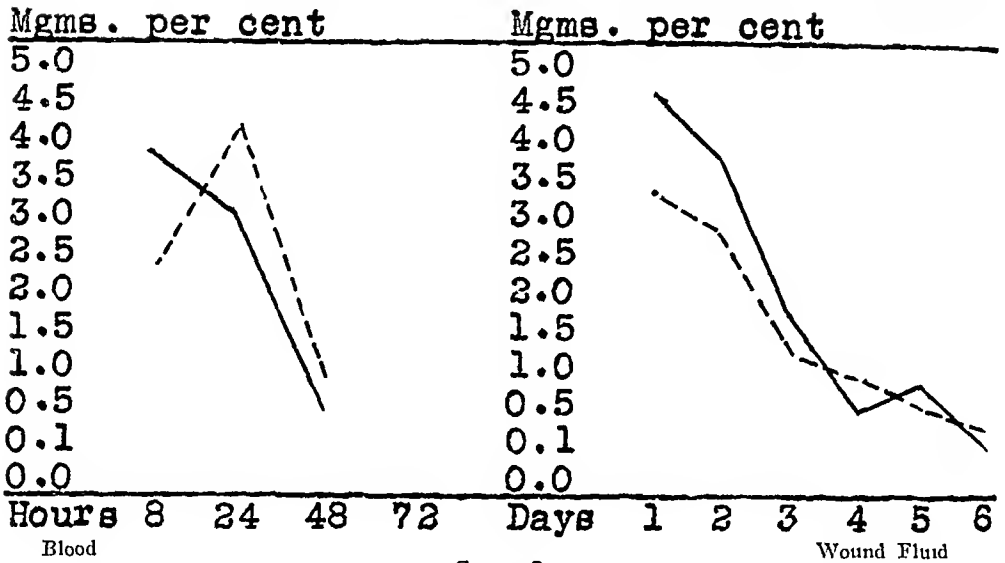


CHART I

Average of Blood and Wound Fluid Sulfonamide Concentrations in the Local Application of Sulfonamides in 25 Thoracoplasty Cases
 Sulfanilamide averaged 4.6 grams in wound per 16 cases Sulfadiazine averaged 3.7 grams in wound per nine cases Sulfanilamide indicated by solid line Sulfadiazine indicated by broken line

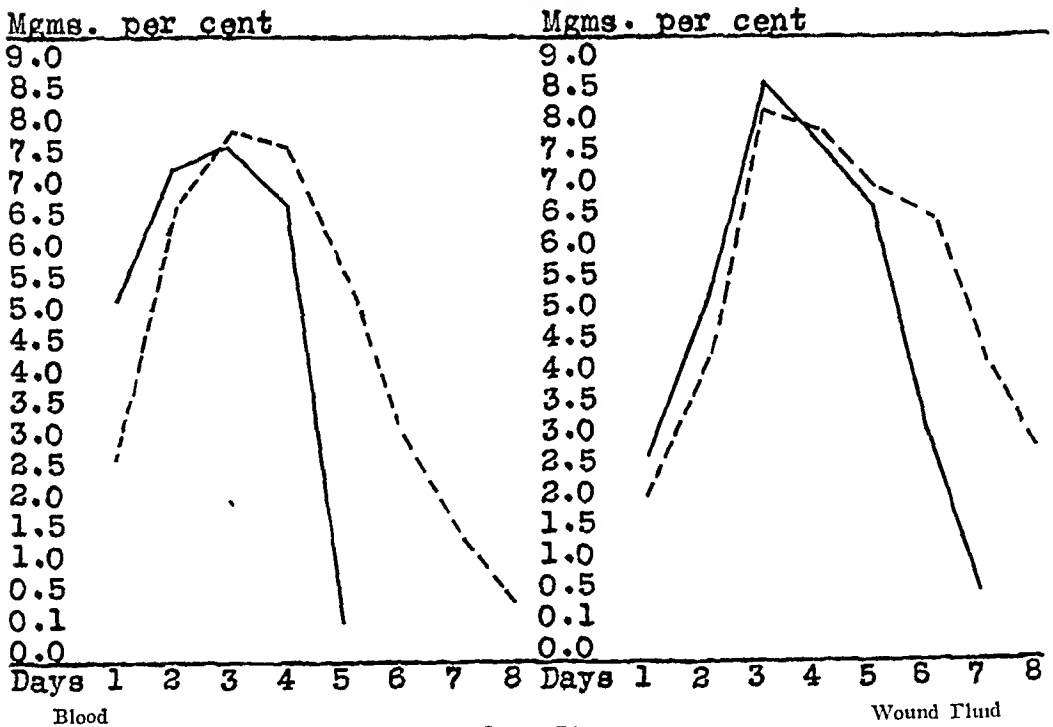


CHART II

Average of Blood and Wound Fluid Sulfonamide Concentrations in the Peroral Administration of Sulfonamides in 21 Thoracoplasty Cases
 Sulfanilamide averaged 20 grams perorally in six cases Sulfadiazine averaged 26 grams perorally in 15 cases Sulfanilamide indicated by solid line Sulfadiazine indicated by broken line

had given satisfactory results in other cases. With this in mind, some of the thoracoplasty cases were given two grams of a sulfonamide by mouth shortly after their operation and then one gram every four hours for three or four days. No case was included if a sulfonamide had been applied locally to the wound. Blood for a sulfonamide level was drawn at the same time that wound fluid was aspirated so that a comparison of the concentrations of the drugs could be made. The data on 21 thoracoplasty cases which received a sulfonamide orally were reviewed and the average blood and wound serum concentrations are shown in Chart II.

The peroral administration of sulfanilamide and sulfadiazine produced good concentrations in the blood stream. The sulfanilamide levels rose and fell rapidly while the peak sulfadiazine levels occurred later and fell less rapidly. Similar concentrations of sulfanilamide and sulfadiazine were found in the wound fluids, but, again, the fall of the sulfadiazine concentrations were slower. The difference in the concentration trends can be explained by the more rapid absorption and the greater diffusibility of sulfanilamide over sulfadiazine. It was worthy of note that the peak wound fluid sulfonamide concentrations as a rule, exceeded the peak blood sulfonamide values. In one unusual case the blood sulfonamide levels reached 81 mg per cent on the fourth postoperative day, while at the same time the wound fluid sulfonamide concentration was 105 mg per cent.

Comparison and contrast of the two series revealed that the local implantation of the sulfonamides yielded immediate high wound serum levels, which rapidly decreased to subtherapeutic values and moderately high blood concentrations that fell even more rapidly, whereas, the peroral administration of the sulfonamides produced, after a short lag interval, high wound fluid and blood concentrations which could be sustained by the oral administration of the drugs. From this it would appear that the immediate, high concentrations of the sulfonamides would be more efficacious than the delayed high concentrations as seen in the oral administration method, but, clinically, less infections occurred when the sulfonamide levels exceeded five milligrams per cent for several days.

The infections in our series of thoracoplasty cases were separated into superficial and deep. The superficial infections occurred above the muscle layers of the shoulder and in the subcutaneous tissues. The superficial infections were mild and never invaded the deeper structures, while the deep infections, which were more severe, occurred beneath the muscle layers of the shoulder and always involved the enlarged, deep subscapular space. Not included in the series were four tuberculous chest wall infections which were believed to have started from a needle tract abscess and one subscapular space infection which followed the rupture of a tuberculous cavity during a revision thoracoplasty operation. These infections delayed or prohibited further surgical collapse measures.

The incidence of pyogenic infections in 203 clean thoracoplasty cases was 5.4 per cent. They range from minor stitch abscesses to severe subscapular

TABLE I
THE SULFONAMIDS USED THEIR MANNER OF EMPLOYMENT AND THE AREAS INFECTED
IN 203 CLEAN THORACOPLASTY CASES

Group	Sulfonamide	Cases	Infections		Per Cent
			Superficial	Deep	
Local	Sulfanilamide	79	3	2	6.3
	Sulfadiazine	13	1	1	15.3
	Sulfathiazole	5	0	0	0.0
Oral	Sulfanilamide	27	1	0	3.7
	Sulfadiazine	12	0	0	0.0
Control	None	67	3	0	4.5
Total		203	8	3	5.4

space infections. The sulfonamides used, their manner of employment and the areas infected are shown in Table I.

The variations in the incidence of infections in the different groups of thoracoplasty cases required further investigation to determine if a greater percentage of wounds in any one group became contaminated. Cultures of the operative wound and the aspirated wound fluid were relied upon as evidence of contamination in lieu of the actual infection and, even then, some were probably missed. The identification of the bacterial contaminants was also desired as a guide to the possible sources of contamination and to the ability of the sulfonamides to prevent specific bacterial infections. We felt that a better evaluation of sulfonamide therapy in clean wounds could be made if the protective ability of the drugs were known.

We reviewed the operative wound, the wound fluid and the infected wound culture reports on the 203 clean thoracoplasty cases and found that 191 were satisfactory for analysis. In the series of 191 analyzed

TABLE II
NUMBER OF CONTAMINATED WOUNDS, NUMBER OF INFECTED WOUNDS AND THE
BACTERIA IDENTIFIED IN 191 THORACOPLASTY CASES

Topics Analyzed in Each Series	Local		Oral	Control	Total
	Sa*	Sd†	Sa	None	
Cases reviewed	73	12	25	64	191
Cases contaminated‡	11	3	4	7	25
Cases infected	5	2	1	3	11
Bacterial contaminants					
<i>Staph. albus</i>	4(0)			2(0)	6(0)
<i>Staph. albus hemolyticus</i>	1(1)	1(1)	1(0)	2(1)	5(3)
<i>Staph. aureus</i>	1(1)		2(1)	2(1)	5(3)
<i>Staph. aureus hemolyticus</i>	3(3)	1(1)	1(0)	1(1)	6(5)
<i>Strept. gamma</i>	1(0)	1(0)			2(0)
<i>Strept. beta hemolyticus</i>	1(0)				1(0)

*Sa = sulfanilamide †Sd = sulfadiazine

‡ Contamination determined by cultures or the occurrence of an infection. () Signifies number of infections.

cases, 20 operative wound cultures were reported positive for pyogenic bacteria and four of them had, in addition, a positive culture of the wound serum. One of the four cases developed a deep wound infection, and five of the remaining 16 cases had superficial infections. Two other cases had sterile operative wound cultures, but later had positive wound fluid cultures, and both developed deep wound infections. Three additional

cases had sterile operative wound and wound fluid cultures, but superficial infections occurred in each

The number of contaminated wounds, the number of infected wounds, and the bacteria identified are shown in Table II

The percentage of thoracoplasty wounds which showed contamination were similar except for the groups, local sulfathiazole and oral sulfadiazine. They had no positive operative wound or wound fluid cultures and no infections occurred. Eleven of the 25 contaminated wounds developed infections an incidence of 44 per cent, while a comparison of the sulfonamide treated and the control groups showed they had a similar incidence. A further breakdown of the groups revealed that only one infection occurred in the four contaminated wounds treated with sulfanilamide orally, while two of the three contaminated wounds having a local application of sulfadiazine became infected.

All of the bacterial contaminants were cocci. The staphylococci made up the majority of the bacteria with the *Staphylococci albus* and *aureus hemolyticus* being the most common. Only three streptococcal contaminations were observed and one of these was the hemolytic streptococcus. The identified bacteria suggested that the greatest sources of contamination were the skin, neighboring infected wounds and the nose and throat of the operating personnel. The protective ability of the sulfonamides was the greatest in the streptococcal group and the least in the staphylococcal bacteria, especially *Staphylococcus aureus hemolyticus*. A further estimation of the drug's protective ability was impossible in the small number of cases.

COMMENT—The popularity and the widespread use of the sulfonamides in surgical cases is reflected in the literature. Some publications reported excellent results with the sulfonamides locally, while others stated that the systemic administration was the most beneficial. Many articles advocated the employment of the sulfonamide compounds in contaminated and infected cases, especially the local application in abdominal surgery, while a few recommended it routinely as a prophylaxis in clean surgical cases. Along with the publications of the good results of sulfonamide therapy have appeared articles reporting the unfavorable aspects as drug toxicity, the development of sensitivity reactions and the occurrence of fatalities from the use of the sulfonamides. The evaluation of sulfonamide therapy in clean surgical wounds must cover both sides.

Meleney,³ in 1944, discussed the problems of evaluating drug therapy in surgical infections. He outlined plans for comparing treated cases in which the numerous factors that influence infections in wounds could be grouped so as to satisfy the most exacting biostatistician. For a drug to be remarkable, its action would have to be clear-cut or the results brilliant. The difficulties in executing the plans are appreciated, but until it is done we must rely on clinical experience.

Harrison and Berry,¹ in 1943, analyzed the results of approximately 430 thoracoplasty cases of tuberculosis at Bellevue Hospital which were per-

formed prior to our series. They stated that the local application of sulfanilamide and sulfadiazine was advantageous in preventing wound infections, and they found no ill effects except excess wound serum exudation. We feel that excess wound serum in the thoracoplasty wound is harmful for it discomforts the patient, often produces necrosis of wound edges unless removed, and the removal by aspiration offers another potential source of bacterial contamination.

The data presented by Harrison and Berry was insufficient for comparing the treated and untreated cases, but they did mention that six minor and four deep wound infections occurred in the clean parenchymal group. Two of the six minor and two of the four deep wound infections developed despite local sulfonamide therapy. Two of the four deep wound infections, however, followed the rupture of a tuberculous cavity and perhaps should not be considered in this respect. The combined incidence of infections in the clean parenchymal group of thoracoplasty cases was 3.4 per cent, while in the empyema group which has a higher risk of contaminations, it was seven per cent.

About the same time, Long² reviewed and summarized the use of the sulfonamide compounds in the prevention and treatment of wound infections. He warned that the sulfonamides, which are an adjunct to surgical therapy, should not be relied upon to cover negligent surgical judgment and technic. He stated that important toxic reactions as fever, acute hemolytic anemia, renal complications, and others occurred in the course of systemic sulfonamide therapy about as follows: sulfanilamide 11.9 per cent, sulfapyridine 15.9 per cent, sulfathiazole 18.6 per cent and sulfadiazine 6.5 per cent. He added that sulfadiazine, which produces the fewest toxic reactions, was responsible for hematuria in 1.7 per cent of treated patients, while the next best drug, sulfanilamide, produced an acute hemolytic anemia in about two per cent of treated patients.

Long analyzed the evidence regarding the local effects of applying the sulfonamides in the wound. He found that wound fluid exudation often formed and if the wound was tightly sutured some necrosis may result. He added that some investigators reported an inflammatory response to the drugs which increased with the less soluble sulfonamides. Often, the inflammatory picture simulated foreign body reactions, especially when large coarse crystals or finely powdered drugs that caked were used. In some articles the wound reactions were interpreted as delayed or poor wound healing.

Long believed that the peroral administration of sulfadiazine, with blood concentrations of four to seven milligrams per cent, coupled with the local application of sulfanilamide offered the best chance for the prevention of wound infections. He felt that sulfanilamide's high solubility, its wide range of bacterial effectiveness and the moderately low degree of associated toxicity made it suitable for local use. Similarly, he selected sulfadiazine for its properties of slow diffusion, wide bacterial range and minimal toxicity for

the oral employment. He added that the peroral administration of the drugs could be stopped after five to seven days in the absence of an infection and the topical application need be continued only in open wounds to prevent secondary invaders.

It does not appear logical to subject clean thoracoplasty wounds to routine prophylactic sulfonamide therapy, as only a small portion become contaminated and even a smaller number develop infections. The occurrence of excessive wound fluid with the local application and the occasional toxic reactions with the oral administration of sulfonamide therapy seems more hazardous than the infrequent, severe infections. If contamination of the thoracoplasty wound could be predicted then either the local or the systemic, or a combination of both methods of administering the drugs, might be employed advantageously, but as most contaminations are slight only bacteriologic studies are reliable indicators. Thus, the rationale of employing the sulfonamides in clean thoracoplasty cases revolves around the potential or actual contamination of the wound.

The antibacterial action of the sulfonamides is the most active against the streptococci. All of the sulfonamide compounds are thought to be about equally effective and their selection is determined largely by the properties of the drugs. The bacteriostatic action of the sulfonamides against the staphylococci is less active and some believe that sulfathiazole is the best while others prefer sulfadiazine. In the latter, it is well-recognized that the systemic use of the drug has proved to be effective against the common contaminating bacteria of wounds.

We suggest, that instead of the routine prophylactic employment of the sulfonamides in clean thoracoplasty cases, the drugs be used only in potentially contaminated cases. We believe that local plus systemic therapy is warranted when gross soiling or some other accident happens to contaminate the wound. Wounds that may become contaminated, as those near an infected area, or when an unusual high incidence of contaminations are occurring, should have the drug applied locally and if the cultures are positive, then the systemic administration of the drug can be started. Again, the sulfonamides should be administered systemically if the bacteriologic studies of the wound or wound fluid reveal contamination, or the patient shows evidence of infection as by unusual temperature elevation or localized wound cellulitis. We feel these indications for sulfonamide therapy in clean thoracoplasty wounds are more efficacious and less dangerous than the routine prophylactic employment of the drugs. Certainly, the lessening of contamination, the application of approved surgical technic and the active maintenance of the patient's defense mechanism is of greater importance in the prevention of clean wound infections than is the present use of the sulfonamide compounds.

SUMMARY

The comparison of local and oral sulfonamide therapy in clean thoracoplasty cases revealed some undesirable features not seen in the untreated cases. The excessive wound fluid formation in local and the toxic reactions

in oral therapy were the chief disadvantages. The local and the peroral employment of the sulfonamides produced predictable drug concentration trends in the blood and the wound serum. The first was immediate and short, while the second was delayed and sustained. Infections followed contaminations in each series, the lowest being in oral sulfonamides, then the controls and the highest was local sulfonamides. The logic of employing the sulfonamides in clean thoracoplasty cases was discussed and our suggestions for the use of the drugs were outlined.

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The selected essay (or essays) will appear on the program of the forthcoming June meeting of the American Urological Association.

Essays must be in the hands of the Secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis, Tennessee, on or before March 15, 1945.

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CRANIOCEREBRAL WAR WOUNDS

OBSERVATIONS ON DELAYED TREATMENT

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AND

CAPTAIN GEORGE E ROULHAC, M C , A U S

ST LOUIS, MO

THIS REPORT is based upon the experiences which we have encountered with severe head injuries, which have been admitted directly to a General Hospital in the North African Theater of Operations, or which have reached here through the usual channels of evacuation. There have been 130 cases of fracture of the skull, of which 74 have been battle casualties, and the remainder due to accidentally incurred injury. Although the number of cases of open head wounds which have been selected as a basis for this report is admittedly small, the cases which are cited illustrate some of the problems of treating this type of injury. Several case histories will be given in detail to demonstrate the fact that treatment, however long delayed, may still be expected to yield satisfactory results. We shall confine this report to facts which we ourselves have observed, and from which we have drawn certain conclusions.

EARLY TREATMENT

The aim of treatment of head wounds, like that of wounds of other regions, is multiple. First, the prevention or eradication of infection in open wounds, second, the preservation of function, or the improvement of physiologic defects resulting from the injury, third, the restoration of anatomic structure as completely as possible. Early and thorough definitive treatment with prompt conversion of a bleeding, contaminated, potentially infected, open wound, into a dry, clean, closed wound, remains the ideal for which to strive, and the following cases illustrate this point.

Case 1—Age 23, a prisoner of war, was shot by a rifle bullet on August 10, 1943. At a Station Hospital 45 minutes after injury, a diagnosis of compound fracture of the right parietal bone was made. Sulfanilamide powder and dry dressings were applied, and the patient was transferred here 10 hours later. After shaving the head, examination showed a wound of entry in the posterior parietal region, with the wound of exit about 6 cm anteriorly. From the wound of exit, there oozed brain and bloody fluid. Roentgenograms showed a comminuted fracture with multiple indriven fragments (Fig 1). There was left hemiparesis. Operation was performed 13 hours after injury. After excision of the wound of entry and exit, a partial horseshoe skin flap was reflected,

exposing comminuted depressed fracture of the upper part of the parietal bone. Bone edges were rongeured and all loose bone was lifted out. There was a laceration of the dura, 3 cm long by 1 cm in width. Several fragments had penetrated to a depth of



FIG 1—Case 1. A, Lateral, and B, anteroposterior views showing fracture of the right parietal bone with indriven comminuted bone fragments.

2 cm. All fragments and macerated brain tissue were removed. The involved area lay chiefly in the arm center. All bleeding points were coagulated. The dura was closed with temporal fascia transplant. The rest of the wound was closed in layers with silk, without sulfonamide or drainage. The postoperative course was smooth. The wound healed *per primam*. The patient was allowed up on the 10th day. Neurologic examination showed residual left facial weakness, and weakness of the left hand with loss of fine movements. He was transferred to the Prison Section on August 28. On October 15, 1943, reexamination showed considerable improvement in skilled movements of the left hand.

Case 2—Age 23, was not a case of gunshot wound, but the problem involved differed not at all from that found in tangential perforating wounds. On September 1, 1943, he was struck in the head by the edge of a log protruding from a rapidly moving truck. At a Station Hospital the head was shaved, and sulfamilamide crystals and dry



FIG 2—Case 2. A and B. Extensive fracture of right parietal and frontal bones, outlined by arrows, with indriven bone fragments, and elevation of one large fragment (B).

dressings were applied to the compounded right frontal wound. He was treated for shock, and transferred to this hospital 20 hours later. Examination on admission showed a ragged laceration about 10 cm long over the right frontoparietal region, from which bone fragments and brain were protruding (Fig 2). There was left hemiplegia and inability to rotate eyes to the left. Twenty-one hours after injury, operation was performed by Major S. P. Haibison. After excision of the skin edges, the wound was extended inferiorly and superiorly, to obtain adequate exposure. Multiple bone fragments were removed, several fragments projected deep into the brain. Macerated brain tissue was sucked out to a depth of 4 cm. Hemorrhage was controlled with coagulation and muscle stamps. The dura was closed with temporal fascia transplant. The rest of the wound was sutured in layers with silk, without sulfonamide or drainage.

The first few days after operation were stormy, with periodic episodes of increased blood pressure and restlessness. Hypertonic fluids were used to good effect, with daily normal fluid intake being restricted to 1500-2000 cc. Beginning about six days after operation, the patient's course improved steadily, and he became oriented and rational. The wound healed *per primam*. Left hemiplegia persisted, but the left leg recovered sufficiently to allow the patient to start walking on the 26th day. The defect was depressed, soft, and pulsating freely. He was sent to the Zone of Interior on October 27, 1943.

Case 3—A French soldier, age 31, was shot by a rifle on May 16, 1943, and reached this hospital one hour after injury. There was a perforating wound of entry in the left lower frontal region, the bullet traversed tangentially, coming out through the tragus and pinna of the left ear. Bleeding was profuse from both wounds. This right-handed patient was not unconscious and had no speech disturbance, astereognosis or apraxia. Except for hyperactive knee-jerks, neurologic examination was negative. Blood transfusion was prepared, and operation was begun three hours after injury. The wound edges were excised and the entry and exit wounds were connected by incision through skin and temporal muscle down to bone. Depressed, comminuted fragments of the frontal and temporal bones were lifted out. A dural tear was enlarged and the underlying macerated brain was sucked out. Bleeding was controlled by silver clips and muscle stamps. The dura was closed, and the remainder of the wound was sutured in layers with silk without drainage and without sulfonamide. The postoperative course was satisfactory. Head and ear wounds healed *per primam*. On June 2, 1943, 16 days after operation, neurologic examination was negative, the patient was up and about, and he was discharged to the French authorities.

Case 4—Age 30, was injured by shell fragments on February 7, 1943. He was admitted to a British General Hospital three hours later, with a severe compound fracture of the left frontal bone, and bleeding from the left nostril. Immediate operation was performed, through a frontal skin flap. Fragments of frontal bone were removed and the frontal sinus was curetted out. Through a laceration of the dura, the damaged tip of the frontal lobe, "the size of a tangerine," was sucked out. All bleeding was controlled by coagulation. The dura was closed with a fascial transplant, and a muscle tampon was placed over a defect in the cribriform plate. Sulfanilamide powder was applied extradurally and the wound was closed without drainage. The patient was allowed up on the 12th day after operation, and evacuated to the rear on the 19th day. He arrived at this hospital on March 2, 1943. The left frontal wound was well-healed, and pulsated freely. There was complete amaurosis of the left eye with primary optic atrophy. Neurologic examination was otherwise negative. The patient was perfectly well until March 12, when he developed cerebrospinal rhinorrhea. He was kept in a sitting or upright position, fluids were forced, and sulfadiazine was given prophylactically. Rhinorrhea ceased on March 18. There were no signs of infection or aerocele, and he was discharged to the Zone of Interior on March 30, 1943.

In cases of acute head injury seen early by us, tight closure without drain-

age and without local sulfonamide has been the rule. Sulfadiazine is given orally or parenterally as prophylaxis only in those cases in which infection is suspected, particularly in wounds which communicate with the nasal or accessory sinuses, *e g*, Case 4.

Case 4 illustrates the effectiveness of early and thorough treatment of a severe head wound complicated by penetration of the frontal sinus and cribriform plate, and loss of dura. The treatment of the subsequent cerebrospinal leak followed well-established principles. Had the leak persisted, or had an increasing aerocele developed, secondary craniotomy would have been necessary.

DELAYED DEBRIDEMENT

Patients with head wounds who may be expected to survive, tolerate transportation quite well, and delayed but thorough treatment is to be preferred to early incomplete measures. Early in the North African campaign we were faced with the necessity of doing long-delayed débridements. Since then we have found that this procedure may be expected to yield satisfactory results, although undoubtedly not as good as would ensue from more prompt definitive care. Conversely, we have been impressed with the complications that may arise if reliance is placed upon inadequate early treatment.

The establishment of any arbitrary time limit within which definitive therapy may be carried out is not necessary. Early débridement and closure should always remain our goal. However, it should be noted that, with the exception of the few cases with dangerous compression due to hemorrhage or a very large depressed fracture, hasty, urgent, inadequate surgery is not usually demanded in head wounds. Unless there is at hand a surgeon familiar with the technical aspects of the treatment of these injuries, and unless he has available sufficient equipment with which to control bleeding, plus satisfactory assistance and the facilities to care for these patients for several days after operation, it is questionable whether any radical procedure should be attempted. The desirability of having such equipment as suction, silver clips, and/or electrosurgical unit for hemostasis, cannot be over-emphasized.

In our series, there have been eight cases in which debridement with closure was done between 36 hours and four days after injury, with primary healing. Additional cases, some of whose records follow, were operated upon and closed after a much longer interval (one as late as 32 days) with surprisingly good results.

Case 5—Age 29, was injured by a mortar shell fragment on March 24, 1943, sustaining a compound fracture of the left parieto-occipital region. On the day of injury, the wound was "debrided" at a Surgical Hospital, with removal of bone chips and copper fragment. Sulfanilamide was placed in the wound, and the galea and skin were closed in layers. The patient reached here on April 8, 1943. The left parieto-occipital wound was incompletely healed, there was one small area which communicated directly with underlying necrotic brain. There was early papilledema. The left pupil was larger than the right. Repeated visual field examinations by Capt E B Alvis, revealed right homonymous hemianopsia with macular sparing on the right.

Hyperreflexia with ankle clonus was present, without pathologic toe signs. There was minimal nominal aphasia, no alexia or agraphia. Roentgenograms showed multiple indriven fragments in the occipital region (Fig 3). On April 14, (21 days after injury) operation was performed under local anesthesia. The entire incompletely healed scalp wound was excised. There was a long narrow bone defect through which necrotic brain extruded, this was enlarged to expose the edges of lacerated dura around the periphery. Necrotic brain, old blood clots, numerous bits of hair, and multiple small fragments of bone were gently sucked out until the edges of the lesion were reached. Several pieces of bone, with accompanying hair, were found to have perforated through the wall of the ventricle, and on removing them there was a gush of ventricular fluid. All damaged brain was removed. The defect involved most of the occipital



FIG 3—Case 5. A and B. Wound of left parieto-occipital region, with extensive destruction of occipital lobe by bone fragments (arrows) driven in to the midline. In this case, the ventricle was penetrated by loose bone and particles of hair. Delayed debridement, with tight closure, was carried out.

lobe, extending medially to the midline, inferiorly to the second temporal convolution, posteriorly only a small bit of brain tissue overlying the tentorium was uninvolved, anteriorly the defect extended to the posterior horn of the left lateral ventricle. Bleeding was controlled by hot saline packs. One large vessel near the surface was clamped and ligated with silk. After the field was dry, the defect was filled with saline. The thickened galea was split, giving an extra layer for suture, and the wound was closed without drainage.

The patient was given a course of sulfadiazine by mouth, and the postoperative course was perfectly smooth. The wound healed by first intention, and the papilledema subsided promptly. Examination after operation showed complete splitting of macular vision, but there was decrease in the blind spot on the left with some improvement in the peripheral field. All other neurologic abnormalities regressed and he was able to be up and around on the 10th day. He was discharged to the Zone of Interior on May 15, 1943.

Case 6—Age 23, sustained a penetrating shrapnel wound of the right fronto-temporal region on March 24, 1943. "Debridement" was performed within three hours at a Treatment Station, where it was noted that brain tissue protruded from the wound. Sulfanilamide was applied and the wound was closed. At an Evacuation Hospital the next day, roentgenograms showed a metallic fragment in the left parietal region, this was wisely left alone. The patient reached here on March 31, 1943. The sutured wound of entry was infected and swollen. Neurologic examination was negative except

for a dilated right pupil, with ptosis and partial ophthalmoplegia. Roentgenograms showed a depressed bone fragment at the point of entry on the right, and a metallic foreign body at a depth of 5.5 cm in the left parietal region. Because of the swollen wound and retained bone fragments, operation was performed on April 1, eight days after injury. The original wound was completely excised. Through a defect in the anterior part of the temporal muscle, a tract led down to the opening in the bone. Two pieces of bone were lifted out, beneath them lay false dura. Anteriorly unhealthy granulations and necrotic tissue were found and removed. Sulfanilamide crystals were sprinkled in the wound outside the false dura, and closure was done in layers, using fine catgut in this case for the temporal muscle and subcutaneous tissue.

The wound healed *per primam*. The third nerve palsy cleared rapidly. On April 4, the pupils were equal and reacted well, extraocular movements were well-performed, but some weakness of the levator palpebrae remained. The patient was discharged to the Zone of Interior on April 17, 1943.

Case 7—Age 20, was struck by aerial bomb fragments on July 6, 1943. At an Evacuation Hospital, immediate debridement was done, with removal of bone fragments and necrotic brain, with primary closure. The wound of entry in the right frontotemporal region was small. Proptosis of the right eye developed. The patient arrived here on July 17, 1943. He was manic, irritable, and uncooperative, there was no power of reasoning or judgment. The slightest stimulus sent the man into a frenzy of screams and obscenity. His behavior was thoroughly uninhibited. There was a healed 5-cm wound in the lower right frontal region. The bulbar conjunctiva was edematous and protruded between the lids. After retraction of the conjunctiva, the cornea was found to be cloudy, and vision in the right eye was absent. The left optic disk was hazy. Neurologic examination was otherwise negative. Roentgenograms (Fig 4, A and B) showed a bony defect in the right frontotemporal region, the roof of the right orbit was crushed, and numerous bone fragments could be seen lying in the frontal lobe as well as within the orbit. There was a metallic foreign body near the surface of the left frontal lobe. There was no improvement during a week's observation.

On July 26, 1943, 20 days after injury, bilateral craniotomy through a Souttar incision was carried out (Fig 4 C). The original wound of entry was used as one of the openings for the right bone flap. Extradural dissection was begun anteriorly. When the orbit was reached, a large dural defect was visualized, and necrotic brain welled up into the field. This was sucked out and the dissection was carried down to the optic chiasm. Many fragments of bone were found within the necrotic tip of the frontal lobe, and the roof of the orbit was shattered back to the optic foramen. These fragments were removed, relieving pressure on the orbital capsule. The optic nerve between the foramen and chiasm was intact. After the field was dry and clean, a transplant of temporal fascia was sutured in place to close the large dural defect. On the left side, exposure of the frontal lobe revealed adhesions between cortex and dura, on the surface of the cortex there was an area of yellow discoloration, in the center of which was a thin layer of necrotic brain covering the underlying foreign body. The fragment, together with the surrounding damaged brain, was excised *en masse*. The dura was sutured, and after replacing the bone flaps the wound was closed in layers with silk. Skin sutures were removed on the second day. The wound healed *per primam*, and the postoperative course was most gratifying. Proptosis disappeared. The patient became clear, rational, and cooperative, judgment, insight, and calculation were restored. He had no recollection of his earlier behavior. On August 17, the atrophic right eye was removed by Capt. Alvis. On September 6, 1943, he was returned to the Zone of Interior with no demonstrable neurologic abnormalities. A letter written September 23, reported him to be in excellent state.

Case 8—Age 21, was struck a glancing blow by a shell fragment on July 12, 1943. First treatment consisted of dressing, without debridement, he received sulfadiazine by



FIG 4—Case 7. A, lateral view, before operation, showing bone defect (wound of entry) in the inferior part of the right frontal bone. In B, postero anterior view, roof of the right orbit is smashed and the orbit is filled with numerous bone fragments (arrow) many of which have penetrated the frontal lobe. The retained metallic foreign body is visualized in the left frontal lobe. C, postero anterior view, after operation, the foreign body has been removed from the left frontal lobe, and the bone fragments have been removed from the right frontal lobe and orbit. (Compare with B). Out lines of the frontal bone flaps are seen.

mouth The patient arrived here on July 26, with his original dressing in place There was a dirty, sloughing wound of the left frontal region, about 4 cm in diameter Roentgenograms showed a comminuted, depressed fracture of the left frontal bone, with two small foreign bodies The wound was so grossly contaminated that preliminary wet dressings were applied

On July 28, operation was performed, with excision of the skin and debridement of the compound fracture Bone fragments and the metallic foreign bodies were removed An extradural clot, 1 cm thick, was found over the anterior part of the frontal lobe, and was evacuated The dura appeared to be intact, although it may have been torn originally After repeated flushing with ether and saline, a thin layer of sulfanilamide was dusted on the dura By means of a short releasing incision, the wound was closed without drainage Postoperatively the patient received a course of sulfadiazine by mouth On August 5, seven days after operation, the wound was completely healed except for a tiny area in the center which was not covered with epithelium, evidently due to too much tension This area, about 2 Mm long, was fully healed on August 10 On August 25, 1943, the patient was discharged to a Convalescent Hospital

Case 9—Age 30, a prisoner of war, was wounded about April 23, 1943 He was first seen at one of our Evacuation Hospitals on May 1, at which time was described a large, gaping wound of the left parietal region "obviously a week or so old" The wound was dusted with sulfanilamide and left open He arrived here on May 11 Examination showed a 2-inch wound with infected cerebral hernia extruding There was partial motor aphasia and right hemiparesis, no astereognosis The hernia was treated conservatively and became partially epithelized, but there continued to be a small amount of purulent drainage

On June 14, the partially healed wound was completely excised to expose the edges of the bone defect Through the defect, necrotic brain was sucked out down to intact tissue Within the involved area were two small bone fragments No frank pus was seen After complete toilet of the wound, the scalp was mobilized by undermining and the galea and skin were closed in layers with silk The wound healed *per primam* Neurologically, there was slow improvement in speech and hemiparesis The patient's mental agility was superb, and he was able to defeat his comrades and attendants regularly at chess He remained in the Prison section until October 8, 1943, when he was repatriated as a walking case

Case 10—Age 26, was struck in the right parietal region by a bomb fragment on February 18, 1943 Because of the tactical situation, surgery could not be performed during his course of evacuation He arrived here on March 2, 1943 Examination showed a tiny puncture wound in the right posterior parietal region, with sanguineo-purulent drainage Roentgenograms showed a superficial metallic foreign body with a small depressed fracture There was tenderness over an area 5 cm in diameter Neurologic examination was negative On March 6, 1943, debridement was performed, with evacuation of bone fragments and a moderate amount of pus The dura was intact The wound was packed open with iodoform gauze It granulated slowly, and secondary closure was done on April 8 The patient was evacuated to the rear on April 21, 1943, with his wound completely healed

Case 11—Age 23, received a shrapnel wound of the right parietal region on July 11, 1943 At a Provisional Surgical Hospital, the compound fracture was "debrided," and brain tissue removed The wound was packed open with sulfanilamide powder and vaselined gauze On July 20, he reached a Station Hospital where a firm pack was removed, revealing a cerebral fungus There was early choked disk and left hemiparesis The patient was operated upon by a neurosurgeon nine days after injury After debridement, with removal of many bone fragments, sulfanilamide powder was sprinkled into the wound, and it was closed around a Dakin's tube The wound healed promptly, and the patient was transferred to this hospital on August 9, 1943 The

wound was well-healed. Eye grounds were normal. Left hemiparesis was slight. The patient continued to show steady improvement and he was sent to the Zone of Interior on August 17, 1943.

Case 12—Age 23, received penetrating wounds of the head and abdomen from a land mine explosion on August 7, 1943. He was treated for shock, and celiotomy was performed four hours later at an Evacuation Hospital, there was no visceral perforation. His condition was too precarious for further surgery, and nothing was done to the left occipitoparietal wound except dressing with sulfanilamide and vaselined gauze. He was evacuated on August 12, and arrived here on August 29. *En route*, records of three medical installations noted exudation of pus and bone fragments from the wound. On admission here, there was blurring of the left optic disk with fullness of the



FIG 5—Case 12. A and B. Very extensive fracture with small wound of entry (arrow) in the left parieto-occipital region. Lines of fracture extend through the parietal to the anterior part of the frontal bone. There are two large fragments which have been elevated, and numerous smaller fragments driven deep into the occipital lobe. There is a large metallic foreign body just to the left of the midline. At operation, two pockets of pus were encountered, one around the metallic foreign body, and the other surrounding the indriven bone fragments. Treated by radical debridement and closure.

retinal vessels. There was right homonymous hemianopsia with some macular sparing. The patient was oriented, but had nominal aphasia, alexia, and agraphia. There was weakness of the extremities, with unsustained bilateral ankle and patellar clonus, and pathologic toe signs on the right. Position sense on the right was partially lost. In the left occipitoparietal region, there was a puffy, tender area, about 6 cm in diameter, with a 2 x 3 cm wound above the pinna of the ear. Foul, thick pus exuded through the wound. Roentgenograms showed extensive fractures of the left parietal and frontal bones, there were many bone chips driven deep into the brain beneath the defect, and a large metallic fragment in the region of the superior longitudinal sinus, just to the left of the midline (Fig 5). While the patient was being built up generally, drainage from the wound continued. Repeated visual field examinations by Capt Alvis, confirmed the macular sparing.

Transfusion was given preliminary to operation, which was performed on September 9, 32 days after injury. A left parieto-occipital skin-galeal flap was reflected, which included the draining entry wound near its center. Necrotic brain oozed from between multiple fractured fragments which were denuded of periosteum. The fragments were lifted out and bone edges rongueured away until the peripheral edges of dura were exposed. Through the large dural defect, pus began to exude from the inferior as well as the superior portions of the parieto-occipital region. Surface vessels, of as yet intact areas of cortex, were coagulated and the entire lesion was uncapped. There was one large abscess in the lower part of the field. This was evacuated, and

from its depths multiple small bone fragments were removed. Another abscess lay superiorly. This was sucked out, and within its medial wall was found the metallic foreign body which was seen roentgenographically. The piece of metal touched the wall of the longitudinal sinus but had not penetrated it, and was removed. It was clear that the falx formed the medial boundary of the superior abscess. Between the two abscesses lay a mass of necrotic brain. This was removed by suction and found to extend to, but not through, the ventricle wall. Both abscess cavities and the intervening bridge of necrotic tissue were converted into a single saucer-shaped defect, 4 cm wide, 7 cm long, and 5 cm deep, extending from above downward along the posterior part of the parietal lobe, with the falx medially and the petrous ridge inferiorly. Marsupialization would have been the procedure of choice on the basis of good surgical principles. However, since the approach had been made through a horseshoe-shaped incision, it was feared that a longitudinal incision through the center of the flap would jeopardize the blood supply of the anterior half. Accordingly, after toilet of the defect, the wound of entry was excised and closed, and the skin-galeal flap was sutured in layers, without local sulfonamide or drainage. It was thought that if abscess recurred, the entry wound could be reopened for drainage if necessary.

Sulfadiazine therapy was begun immediately after operation. The wound healed *per primam*. The postoperative course was uneventful and the patient was allowed up on the 10th day. The defect remained depressed and pulsated freely. Neurologically, there was slow but definite improvement. Blurring of optic disks disappeared. Visual fields showed no change. Visual acuity was 20/20 in both eyes. Nominal aphasia improved considerably. Alexia was marked but improved so that monosyllabic words could be read. There was definite acalculia. Skilled movements of the right hand were slightly less well-performed than on the left. Position sense of the arms was intact. The right lower extremity was slightly spastic with hyperactive knee jerk, no clonus or pathologic toe signs. Position sense of the right toes and ankle was absent. Fine discriminatory sense was absent over the entire right side of the body except for the head and neck, other sensation was intact. The heel-knee test was uncertain bilaterally. With the hands outstretched and eyes closed, the right arm drifted upward. The patient was able to walk well with eyes open, but with eyes closed, lack of position sense of right foot became apparent. He was discharged to the Zone of Interior on October 27, 1943.

Cases 5 (21 days), 6 (8 days), 7 (20 days), 8 (16 days), 9 (51 days), and 12 (32 days) are illustrative of what may be expected in some cases of head wounds even if they are allowed to go for a very long period of time before receiving adequate débridement, and are then subjected to radical débridement, with tight closure, without drainage. This is not to be misinterpreted as meaning that tight closure is the procedure of choice in all cases. The surgeon must apply his own judgment to each individual case. For example, in instances where there is gross infection and it is obvious that complete cleaning out of the wound cannot be accomplished, drainage is essential. The wound in Case 11 was closed around a Dakin's tube which was left for two days. In Case 10 the wound was packed open with iodoform gauze because of the extensive area of subcutaneous swelling and tenderness and the fear of spreading osteomyelitis. In this connection, it may be noted that, in our experience, spread of osteomyelitis in the skull is far less likely in battle wounds than in civilian practice where hematogenous infection occurs.

The good result in Case 5 is particularly significant in view of the long delay and the fact that the ventricle was penetrated by bone fragments and

hair The procedure followed in Case 12 may be open to justifiable criticism This defect presented every indication for drainage, containing as it did two pockets of pus and having discharged pus for over four weeks The reasons for not draining have been given in the description, and through fortuitous circumstance, the case now stands as an extreme illustration of what may be accomplished with late débridement and tight closure in at least this instance

As a rule, we have not used sulfonamide locally, even in late cases, but have given large doses parenterally and by mouth, checking blood concentrations daily Usually, immediately after operation, the patient receives either six grams of sulfanilamide subcutaneously, or three grams of sodium sulfadiazine intravenously The latter is repeated after four to six hours In practically every case it has been possible to give one gram of sulfadiazine by mouth every four hours, beginning about 12 hours after operation The six grams per day oral medication is continued for four days in the ordinary case (blood and urine being checked), after which time the dosage is decreased by two grams daily

Emphasis should be placed upon adequate débridement Débridement as a descriptive term is unhappily used somewhat loosely The foregoing histories are a few that serve to illustrate the fact that incomplete débridement is usually ineffective It is urged that, even if time is lacking, the surgeon should qualify the term débridement so that more rapid evaluation of the requirements of individual cases may be made as soon as they reach an installation where definitive surgery is available

If débridement cannot be done adequately in early cases (and it should again be pointed out that physical facilities and equipment cannot be overestimated) it is better simply to shave the head and apply a snug, dry sterile dressing to the wound with sulfanilamide crystals superficially, and transport the patient to the rear, fortified with sulfonamide medication by mouth

FASCIAL TRANSPLANTS

In our acute cases we have made every effort to restore anatomic relations whenever possible, and have used fascial or periosteal transplants when necessary to close dural defects In later cases, unless one can be absolutely certain of the completeness of the débridement, it would appear to be unwise, and we have not closed the dura in such instances The following cases, done elsewhere, are cited The first with successful outcome, and the other two associated with complications

Case 13—Age 24, was struck in the left parietal region by a fragment of enemy antiaircraft shell on April 19, 1943 The wound was excised and metallic foreign body was removed at a Clearing Station two and one-half hours after injury He was evacuated to a General Hospital (British) where a secondary débridement was done on April 21 A bone fragment and necrotic brain tissue were removed A periosteal graft was used to close the dural defect and the wound was closed tightly in layers

Recovery was uneventful. The patient arrived here on May 9, at which time neurologic examination was entirely negative, and the head wound was solidly healed. On May 15, 1943, he was sent to the Zone of Interior with the expectation of subsequent return to full combat duty.

Case 14—Age 21, was struck in the right frontal region by enemy rifle fire on August 7, 1943. He was able to walk to an Aid Station, where his wound was dressed and he was given sulfanilamide. Due to local conditions, he did not reach a Field Hospital until August 9. Roentgenograms there revealed a right parietal fracture, with numerous foreign bodies at the site of fracture. He had a left hemiplegia, and brain tissue extruding from the wound. On August 10, three days after injury, operation was performed. After removal of macerated brain and bone fragments, the dura was



FIG 6—Case 14. A and B. Showing large bone defect in right frontal bone, with some deep, retained bone fragments. This patient had had a fascial dural graft three days after injury, followed by infection and development of cerebral hernia.

closed with temporal fascial graft, local sulfanilamide, closure in layers. He was removed to a General Hospital on August 16, where it was noted that the right frontoparietal wound was broken down and exuding pus. The patient was sent to a Station Hospital on August 22, and subsequently arrived here on August 29. Examination showed a dirty semilunar wound, right frontal, with granulations and pus extruding. There was left facial weakness. The right optic disk was blurred and there was cervical rigidity. Roentgenograms here showed multiple linear fractures with a 6 x 2.5 cm defect of the right frontal bone. Bone fragments were visualized in the brain as well as some metallic fragments at the posterior aspect of the defect, just within the inner table (Fig 6). On August 30, operation was performed. The semilunar incision, through which projected three small cerebral fungi, was reopened, exposing bulging infected brain and a large piece of necrotic fascia, partially attached by multiple silk sutures. The sloughing fascia was removed together with the sutures. There were three separate points draining pus. The bulging mass of infected brain was excised with the electrocautery, exposing in the course of excision several small pockets of pus which were evacuated. Several pieces of bone were found and removed. The underlying brain was necrotic and obviously the seat of spreading infection, this was sucked out. The wound was packed open with a Mickulicz drain. He was placed on a course of sulfadiazine immediately.

Following operation, meningeal signs promptly disappeared, and the optic disks, previously blurred, became clear. The exposed brain began to granulate over, and the

skin flap became firmly attached except at the lateral margins. On one occasion it was felt that there was a communication with the ventricle which sealed over. A small point of drainage persisted. This was injected with diodrast and was found to extend down for about 2 cm, and there was evidence of osteomyelitis at the lateral bone edge. On October 15, the skin flap was reflected back, and osteomyelitic bone was rongeured away. The wound was again packed open. Sulfadiazine was given by mouth. The exposed brain became epithelized promptly and the defect was covered with solid epithelium except for a tiny area in the center which was almost healed when the patient was evacuated on November 20.

Case 15—Age 31, was struck by mine fragments on August 3, 1943. At a Clearing Station that evening, a diagnosis of compound fracture of the left frontal bone, with herniation of the frontal lobe, was made. At operation, the defect was smoothed, hemorrhage controlled, and devitalized brain removed with bone fragments. The wound was packed with sulfanilamide and vaselined gauze. He went through a Field Hospital the next day and reached an Evacuation Hospital on August 5 when reoperation was undertaken. According to the accompanying notes a cerebral fungus was resected, requiring "left frontal lobectomy", a large foreign body was removed. Sulfanilamide powder was placed in the wound. The dura was closed with a fascial graft from fascia lata. Sliding graft was necessary for scalp closure. He was placed on sulfadiazine and his condition was noted as satisfactory when he was evacuated on August 10. He reached here through the chain of evacuation on August 15.

There was foul discharge through the original head encasement. Neurologic examination was negative, speech was clear. On removal of the encasement, there was a pulsating puffy defect with foul purulent drainage. Skin sutures were removed, resulting in profuse discharge of pus. On retracting the skin edges there was a 5-cm bony defect in the center of which lay a loose, sloughing fascial graft. The graft was removed together with silk sutures and the wound was packed open. The cerebral fungus responded well, and in the course of a week began to recede. Skin edges were allowed to epithelize over the periphery of the hernia and it healed completely within six weeks, except for one small area medially, which continued to drain a small amount. Roentgenograms, with diodrast, showed a small invaginated pocket. A tiny piece of retained bone fragment was lifted out and a thin rubber drain was inserted. This resulted in prompt healing. The patient was discharged to the Zone of Interior on October 27, 1943.

The persistent infection which complicated the course in Cases 14 and 15 might have been expected in the presence of retained bone fragments plus the addition of a fascial dural transplant with silk sutures in a contaminated field. They also serve to illustrate the inefficiency of incomplete débridement.

"PACKING" OF HEAD WOUNDS

Cases 11 and 15 were both subjected at first to incomplete débridement with sulfanilamide-vaselined gauze packing. We do not believe that this type of dressing is applicable to head injuries. Just as its abuse has been noted in cases of wounds of the extremities, where tight packing results in damming up of infected tissues, the packing of a penetrating head wound with vaselined gauze (if allowed to remain for long) is equally hazardous, particularly when bone fragments and foreign material have not been removed. The following case illustrates this point.

Case 16—Age 35, received a gunshot wound of the head on February 16, 1943. On the night of the injury he was treated at a Surgical Hospital, where the "scalp wound (was) excised, fracture of skull present, depressed fragments removed, sulfanilamide-vaselined gauze, scalp sutured loosely." He was started on a course of sulfadiazine. The patient arrived here on February 24, 1943. He was confused and irrational. There was

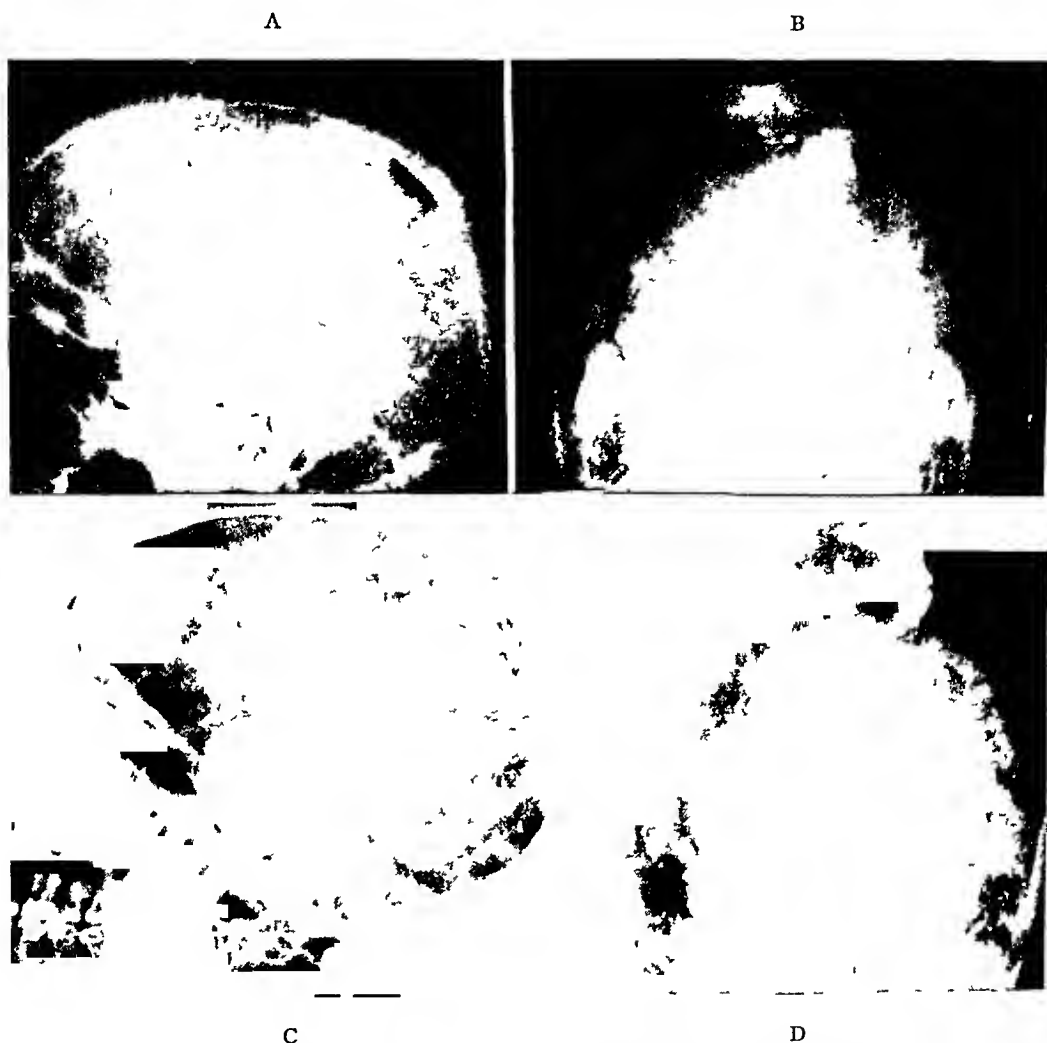


FIG 7—Case 16. A and B. Showing extent of abscess as outlined by radiopaque iodoform gauze drain. C and D. Comparable views, taken two weeks later, the abscess cavity has become much smaller and healing is progressing. This patient had retained bone fragments within the abscess cavity, original wound treated with vaselined pack.

early papilledema. The left shoulder girdle muscles were weak and there was drifting of the outstretched left arm. Neurologic examination was otherwise negative. The edges of the infected right parietal scalp wound were held by two silk sutures, which forcibly restrained a vaselined pack. On removal of the sutures, the pack delivered itself, and the underlying wound showed an obvious central defect through which necrotic brain oozed. Roentgenograms showed a depressed comminuted fracture of the right parietal bone with indriven bone fragments. On February 26, operation was performed. After removal of redundant brain tissue, at a depth of 1 cm a large abscess containing 40 cc of thick creamy pus was found and evacuated. The abscess wall was moderately thick. Several pieces of bone were found and removed from the cavity. Iodoform drains were placed in the abscess and the skin left open. Roentgenograms, with iodoform drains in place, were taken at weekly intervals, and we were

able to follow the healing process visually (Fig 7) There was complete healing of the abscess and the skin on April 2 Neurologic examination showed almost no drifting of the left arm and only slight instability on finger-nose test He was able to walk well Optic nerve heads cleared promptly He was evacuated to the Zone of Interior on April 8, 1943

METALLIC FOREIGN BODIES

The problem of removal of metallic foreign bodies is a difficult one at times These materials are usually not a nidus of infection, whereas retained bone fragments appear to be responsible for infection in most cases The occurrence of an abscess around the indriven piece of metal in Case 12 demonstrates that this cannot be considered a hard and fast rule The following case is cited to illustrate failure on our part to recognize the presence of a large lesion resulting from multiple metallic foreign bodies

Case 17—Age 21, was struck by enemy fire on July 12, 1943 The exact type of missile was not known Operation aboard ship was performed within 12 hours, consisting of débridement, local sulfanilamide and closure of the left temporal wound The patient was stuporous and had partial paralysis of the left face and leg, at least until July 16, when he reached a Station Hospital There the temporal wound was found to be infected, and on July 22, a second debridement was done, with drainage The patient's condition improved and he was evacuated, reaching here on August 8, 1943

Examination showed an infected left temporal wound with a large amount of drainage There was swelling below the mandible with trismus Neurologic examination was entirely negative Speech was clear The partial left facial and leg palsy had apparently cleared up while *en route* Roentgenograms showed a 2.5 cm defect in the squamous portion of the left temporal bone, with two large metallic fragments at the fracture site, there were several smaller fragments intracranially beneath the coronal suture (Fig 8 A)

During the next few days trismus became more marked On August 12 an aneurysm of the internal maxillary artery was found and excised, resulting in relief of trismus The left temporal wound continued to drain profusely Neurologic examination remained negative, with normal fundi Sulfadiazine was given right along, with maintenance of high blood concentration It was thought that persistent drainage was due to retained foreign bodies at the fracture site

On August 20, operation was done The temporal wound was excised down to the anterior part of the pars squamosa A sinus tract ran down to the bone defect Lying in the defect were several loose bits of bone, and buried in the zygoma were several pieces of metal, dirt, and hair All this was removed and the bone edges were rongueured down to healthy bone The dura was covered over with tough scar and there was no evidence of a tract through the dura, at this time The wound was closed loosely around a Penrose drain

Sulfadiazine was continued postoperatively The wound continued to drain Postoperative roentgenograms (Fig 8 B) showed a clean temporal defect, with the previously noted small metallic fragments along the vertex Neurologic examination was consistently negative Eye grounds were checked repeatedly by us as well as by the ophthalmologist, and disks remained flat and clearly outlined Visual fields were full The patient was mentally clear Vital signs were normal He was allowed to get up On September 17, he complained of general malaise and had low grade fever, neurologic examination was negative Malaria was suspected, but no parasites were found on smear On September 18, there was fully-developed meningitis, with temperature 104° F, rapid pulse, and stiff neck The patient became very confused Spinal

A



B

FIG 8—Case 17. A. Lateral view showing several large metallic foreign bodies (arrows) within a ragged frontotemporal defect. Numerous small foreign bodies scattered throughout the frontal lobe. B. After removal of the large metallic foreign bodies and pieces of bone in the defect. This patient developed an extensive brain abscess which was not recognized clinically.

puncture was done, pressure was 220 Mm of water. The fluid was turbid, contained 14,000 cells per cc, of which 90 per cent were polys. No organisms were found on smear. Sulfadiazine was continued. On the morning of September 19, temperature was 99° F, neurologic findings unchanged. At noon he suddenly lost consciousness and died of respiratory failure.

Autopsy showed a narrow tract running through the scarred dura to the temporal lobe. There was diffuse basilar meningitis. The entire left hemisphere felt soft and the gyri in the frontotemporal region were flat and yellow. On section of the brain, a large, thin-walled abscess was found which involved the frontal and temporal lobes, and extended back to the posterior horn of the left lateral ventricle, at which point it had ruptured into the ventricle.

On reviewing this case, there are several significant features. There had been two débridements before evacuation to a General Hospital. After reaching this hospital, despite the large size of the abscess, there were neither general pressure nor localizing signs. As a matter of fact, mental and emotional instability noted on admission here had disappeared, as had the facial and lower extremity palsy which had been observed aboard the Hospital Ship. From the extent of the lesion demonstrated at autopsy, one would have expected aphasia (the patient was right-handed), visual field defect, and at least partial hemiplegia. The infection had evidently progressed with only thin walling-off despite continued sulfadiazine therapy. For our part, we were led astray by the fact that there was no demonstrable tract leading through the scarred dura at the time of exploration of the temporal wound, as well as by the prevailing opinion (which we share) that intracerebral metallic foreign bodies are not often associated with abscess. In our own experience, indriven bone fragments have most frequently been found in association with infection. The persistent discharge of pus led us to suspect, erroneously, that there might be osteomyelitis of the superior margin of the zygoma. In retrospect, despite lack of general pressure and localizing signs, the mistake we made was in not exploring intradurally with a needle. If it was felt unwise to insert a needle through the infected temporal defect, this procedure could have been done safely through a perforator opening in a clean field.

We believe that the removal of indriven bone fragments, with particles of clothing, hair, *etc*, is of paramount importance in all cases. If a metallic foreign body is readily accessible and if its removal does not mean inflicting severe functional damage, then every effort made to effect its removal is justifiable. We do not yet know what incidence of traumatic epilepsy may be expected to occur in this war, in head wounds with retained foreign body and cortical scar. In Case 7 it was believed that removal of the foreign body (Fig 4) which lay near the surface of the left frontal lobe was indicated at the same time that we performed delayed débridement of the right frontal lobe.

Due to the relatively short period in which wounded men remain in the Theater of Operations, we could not expect to encounter many cases of traumatic epilepsy. The following case of jacksonian seizures which came

under our care is cited as our single experience with the condition in this Theater

Case 18—Age 24, was struck by high explosive fragment during an air raid on June 6, 1943. He did not lose consciousness. At a General Hospital (British) two hours after injury, examination showed a small penetrating wound of the right parietal region just above the ear. He had a right peripheral facial weakness, partial flaccid paralysis of the left arm, and absent knee-jerks. Debridement, with primary suture, was performed immediately. The immediate postoperative course was uneventful, and he was transferred to a Station Hospital on June 23. The following day he had a jacksonian fit, beginning in the left hand and arm, spreading to the left leg, and then

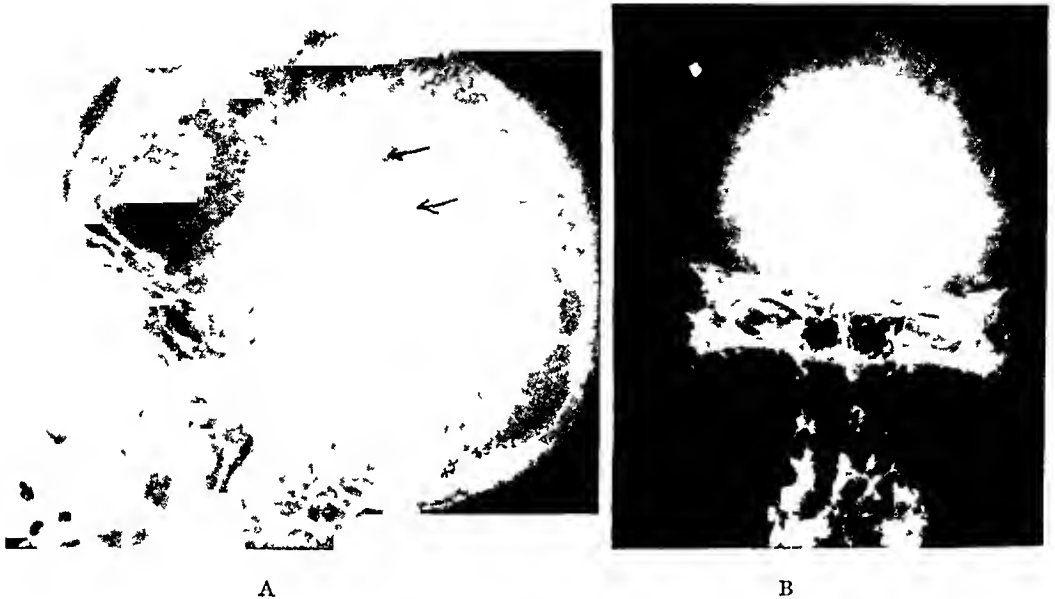


FIG 9—Case 18. A and B. Penetrating wound of right parietal bone with retained bone fragment and metallic foreign body. Patient had jacksonian seizures beginning in the left hand. At operation cortical scar with retained foreign body removed *en masse*.

becoming generalized. He was transferred to a General Hospital on June 25, where the wound broke open and drained a small amount of serous fluid. This healed within a few days, and the patient reached this hospital on July 21. There was a healed incision 3 cm long in the right parietal region, with a small underlying bone defect. The only neurologic abnormalities were astereognosis, ataxia, and lack of fine movements of the left hand. Roentgenograms showed a few loose fragments of bone directly beneath the bone defect and a small metallic foreign body, 1 × 0.5 cm apparently within the cortex (Fig 9). The patient was right-handed.

On July 29, 1943, approximately seven weeks after injury, and one month after the wound was healed, a right parietal craniotomy was done. Through a small bone flap, the original laceration of the dura was found to be covered with tough fibrous tissue which led down through a dense scar to underlying brain. This part of the dural flap was cut out. In the position of the arm area the cortex was yellow and scarred, with the rolandic vein running along the surface. It was possible to peel this vessel away from the lesion and preserve its continuity. Superficial vessels were clipped and cut, and the entire scar with its retained foreign body was removed *en masse*. The defect was 3 cm in diameter and 2.5 cm deep. The wound was closed in layers with silk, using a piece of temporal fascia to close the dural defect. While undergoing anesthesia (pentothal sodium), the patient had tonic-clonic movements of the left arm and leg, but did not go on to general convulsion. On two occasions coagulation of

small vessels at the periphery of the cicatrix resulted in flexion of the left hand and arm, and rotation of the shoulder

On the night of operation, the patient was started on luminal, grains one, three times daily. There was paresis of the left arm and face, the leg was not affected. On the first day, he was able to extend and rotate the arm and hand, and the facial weakness was disappearing. Sutures were removed on the second day, at which time there was no longer any facial weakness, and the arm was improved. The wound healed *per primam*. By the tenth postoperative day arm movements had returned and he was able to manipulate a match box with his left hand as well as before operation. He was allowed up on the 10th day, and his course continued satisfactory. Astereognosis and impairment of fine movements of the left hand were still present when the patient was returned to the Zone of Interior on September 6, 1943. In a letter dated November 1, his sole complaint was sensory impairment of the hand.

In cases in which the retained metallic foreign body is inaccessible, where it is situated in a vital area, the offending fragments should not be disturbed unless it gives rise to abscess later on. Figure 10 shows a metallic fragment



FIG 10—A and B. Films of a soldier with a healed penetrating wound of the right orbit. Several retained metallic foreign bodies the largest of which lies in the midline directly above the sella turcica. There had been transient polyuria and polydipsia which cleared rapidly. No attempt at removal of foreign body indicated.

which entered the right orbit of a soldier on February 27th and lodged over the sella turcica. There had been transient polydipsia and polyuria early, but neurologic examination was entirely negative, and there were no hypothalamic signs or symptoms on arrival here on March 8, 1943. Any attempt at removal of the foreign body would have been disastrous.

The following case demonstrates a problem that may arise from time to time.

Case 19—Age 22, sustained a penetrating wound of the parieto-occipital region on March 28, 1943. There was almost total blindness immediately. On March 31, debridement was performed at an Evacuation Hospital, with removal of bone and metallic fragments from both calcarine areas, "some fragments were inaccessible." At a Station Hospital papilledema was noted on April 10, 1943. He reached here on April 12, 1943. There was a transverse occipitoparietal wound just above the region of the torcula, which was healed except for one area in the center at which point galea was not epithelized.

There was bilateral papilledema. Visual acuity, bilateral, was limited to finger movements at five feet. Roentgenograms showed a defect over the midline posteriorly, there were several metallic foreign bodies including one which appeared to be within the region of the sinus (Fig 11). We believed, with the original surgeon, that removal of the fragments should not be attempted unless absolutely necessary. Aspiration with a needle through intact lateral margin of the defect yielded a few drops of sero-sanguineous fluid, no pus. The eye grounds were checked repeatedly, and papilledema receded gradually, so that there was no measurable elevation by April 24. Visual acuity rose to 3/200 in each eye. Tangent screen examination on May 11, showed right homonymous central field defect with involvement of the maculae. The unhealed portion of the wound healed within a few days. The patient was able to be up and about and was discharged to the Zone of Interior on May 16, 1943. Had signs of pressure persisted, we would have been obliged to remove the shell fragments as a source of infection.



FIG 11—Case 19. A and B. Wound of occipital region, midline, with retained metallic foreign bodies just above the torcular Herophili. Admitted after early incomplete debridement, with choked disks. Under conservative treatment, pressure signs disappeared, and there were no signs of abscess. Foreign bodies were not removed.

Parenthetically, it might be added that an attempted removal of these foreign bodies in the forward echelon, without adequate facilities would have courted disaster.

{CLOSURE OF WOUNDS

In early cases, following débridement, it has been an accepted neurosurgical practice to close the head wound tightly, without drainage. Such closure after careful toilet of the wound will almost inevitably result in primary healing, and will prevent the development of a cerebral hernia, with its long period of morbidity. At times, there has been so much loss of skin that after excision of only a narrow margin, difficulty in closure is encountered. If undermining does not result in sufficient mobilization of the scalp, one may then be forced to use releasing incisions and "sliding grafts." If this procedure is performed, sufficient relaxation must be sought to allow closure without too much tension, and the releasing incisions must be so placed as not to jeopardize the vitality of the primary wound.

We have had to resort to releasing incision in only one case, and in that

instance (Case 8) it is worth pointing out that one part, however small, of the primary wound was not fully healed until the 12th day, this was due to too much tension. The following case is presented as an instance in which laterally placed releasing incisions appeared to have jeopardized the vitality of the central wound, although local infection was probably the main factor.

Case 20—Age 49, was hit by shell fragments on April 23, 1943, sustaining a penetrating wound of the vertex. He was taken to an Evacuation Hospital, where preoperative examination noted "neurological essentially normal, except for semicomatose." Roentgenograms showed a defect in the vertex of the skull, with a metal fragment deep in the right temporal lobe. The wound was debrided on the day of injury, exact time interval not known. The superior sagittal sinus, which ran through the wound, was successfully avoided. Bone fragments were removed, but the metallic fragment was not looked for. The dura was not closed. To close the scalp, two lateral releasing incisions were made. The patient was transferred to another Evacuation Hospital on April 25, where "sensory epilepsy" was noted. At a Station Hospital on April 30, paralysis of both legs was observed. The patient arrived here on May 4, 1943.

Examination showed an area about 6 cm in diameter directly over the vertex, which was red, hot, and swollen. There was a central tripod incision, flanked by two lateral releasing incisions, about three inches long. The three wounds were covered with pus, and the tripod had broken down, with cerebral fungus protruding. From the relative position of the anterior limbs of the tripod and the releasing incisions, it was thought that blood supply to the central wound was not adequate. The patient had terrific paroxysmal pain in both legs. The left leg was completely paralyzed, the right partially so. Both disks were blurred. The right pupil was larger than the left. There was marked incoordination and loss of fine movements in both arms, particularly the left. There were no pathologic toe signs. Sensation was definitely diminished and position sense was absent in both legs.

The head was shaved and wet dressings were applied for a few days to reduce the cellulitis. Fluid intake was limited, although sulfadiazine was given. After cellulitis had disappeared, aspiration with a needle through a clean field was done to rule out possible abscess, no pus was obtained. The bulging hernia was then treated with boric-vaselined dressings. Lumbar puncture was done twice to reduce the protruding mass. After subsidence of the cellulitis and infection, the hernia receded and epithelization began. *Pain passu* with recession of the hernia the patient's condition steadily improved. On June 6, 1943, there was complete healing of the tripod as well as the releasing incisions, and the defect was flat. Disks were normal. The patient was free of pain. Abnormal signs in the upper extremities disappeared. He was able to move all muscle groups of the lower extremities, but was not yet able to support his own weight. There was marked ataxia on heel-knee test. Absent position sense below hips, and loss of fine discriminatory sensation below the costal margin. There was no clonus or pathologic toe signs. The patient was discharged to the Zone of Interior on June 15, 1943.

In late cases, closure may be attempted if there is no massive infection, and if removal of all involved necrotic tissue and retained fragments is accomplished. This has been carried out successfully in cases cited previously. Although it was also successful in Case 12, in the presence of abscess, we realize that this was a risky procedure, and this case would have been more safely handled if drainage had been instituted.

HERNIAE CEREBRI

In a certain number of cases, cerebral hernia is bound to occur. In our series, this complication was noted in either (1) cases incompletely débrided and closed, and broken down by infection, or (2) cases which were so badly infected by the time first medical treatment was available that closure was deemed unwise, or (3) cases which were débrided but were not closed tightly.

Treatment of such herniae is conservative. If superficial infection is taken care of, recession of the hernia with epithelization usually occurs, unless there are retained bone fragments or other material which act as a focus of deep infection. In cases without retained material, we have dressed these wounds with fine mesh, vaseline- or boric ointment-impregnated gauze, after preliminary cleansing with boric acid solution or wet saline dressings. If the hernia is large, lumbar puncture is done to promote recession of the mass. Where bone fragments are retained beneath the surface, there will usually be a draining sinus through the hernia, and prompt removal of the fragments, with drainage, will save time and may prevent more serious complications. If the hernia continues to enlarge and shows no signs of recession, underlying brain abscess should be suspected, and if this is present, should be treated by uncapping the hernia and instituting drainage. It is our opinion that drainage, with removal of contained bone fragments and foreign bodies in the abscess, should be performed promptly.

The following case represents an unhappy outcome due to abscesses beneath a cerebral fungus.

Case 21—Age 24, prisoner of war, sustained a penetrating gunshot wound of the left frontoparietal region on May 5, 1943. Available records began only after his first admission to an American Evacuation Hospital on May 11. At that time, he was aphasic and had right hemiplegia, pulse was slow, the left pupil was larger than the right. The previously sutured scalp wound was infected. Roentgenograms revealed a slight shift of the calcified pineal body to the right and downward. On May 12, the infected scalp wound was opened, with escape of pus and blood. The brain was apparently sealed over and was not disturbed. The wound was left open, with sulfanilamide and vaselined gauze. A left subtemporal decompression was then done. The patient was transferred here on May 20, 1943. Examination showed tense, subtemporal decompression. Near the vertex on the left, there was a cerebral hernia which bulged moderately. There was aphasia and right hemiplegia. On May 26, 1943, operation was performed. The edges of the old infected cruciate wound of the vertex were retracted. Redundant hernia was excised, and at depth of 4 cm, a large multiloculated left frontal lobe abscess, with retained bone fragments, was evacuated and drained with iodoform gauze. Immediately following the procedure, the subtemporal decompression became flat and remained so for a week. With iodoform drains in place, roentgenograms demonstrated apparent healing of the large abscess. Another abscess was suspected in the inferior part of the frontal lobe in the vicinity of a retained metallic foreign body. This proved to be a small one when aspirated through a perforator opening on June 8. The patient received continuous sulfadiazine therapy from May 26 until he died on June 22. Autopsy revealed complete healing of the large multiloculated abscess which was drained on May 26. Throughout the remainder of the left hemisphere, including

the occipital lobe, however, there were multiple small abscesses, with a small amount of pus in the left lateral and the third ventricles

SUMMARY AND CONCLUSIONS

(1) The experiences in the treatment of craniocerebral wounds in a General Hospital in the North African Theater of Operations are presented

(2) Early complete débridement of head wounds, with anatomic closure in layers, and without drainage, is the most desirable type of therapy

(3) Satisfactory results may be achieved by thorough débridement, even when there has been a very long delay. In selected cases, delayed débridement, with tight closure, and without drainage, has been successful after as long as 32 days. The establishment of any arbitrary time limit within which definitive treatment may be given is not indicated.

(4) If facilities for definitive neurosurgical therapy are not available in the forward echelons, it is to the patient's advantage that he be transported to an area where such facilities are available, rather than be subjected to inadequate early treatment. Prior to evacuation, the scalp should be shaved and a sterile dry dressing, with sulfonamide crystals, applied.

(5) Facial transplant for repair of dural defects is hazardous in late cases.

(6) "Packing" with sulfanilamide-vaselined gauze is not applicable to the treatment of craniocerebral wounds.

(7) Retained bone fragments, with or without foreign materials, are the most common source of persistent suppuration, and their removal is almost mandatory. Metallic foreign bodies do not commonly act as a focus of infection, but may do so.

(8) Sulfonamides have been used in the treatment of this group of cases. However, as a rule, we have not used sulfonamides locally, but have given these drugs parenterally and orally.

SECONDARY SUTURE OF WAR WOUNDS

A CLINICAL STUDY OF 305 SECONDARY CLOSURES

LIEUT COL HARWELL WILSON, M C , A U S

DELAYED WOUND CLOSURE in civilian practice is a procedure which is not frequently employed. In the care of battle casualties, secondary closure of the wound plays a vital part in the early return of soldiers to duty. Experiences gained during the past year have reemphasized certain surgical principles involved in the management of these wounds. It is believed that the principles involved in the successful management of war wounds are equally applicable to certain traumatic wounds seen in civil practice.

Adequate débridement without suture of war wounds in the initial stage of treatment is a necessary principle, the importance of which has been repeatedly emphasized.¹ This procedure is necessary because of the extensive devitalization of tissue so frequently found in war wounds, the extensive contamination of such wounds with foreign material, and the time-interval often present between receipt of the injury and the initial surgical treatment. During a period of rapid evacuation of war casualties, it is often necessary for an individual to be cared for by a number of different surgeons within a relatively short period of time. This fact, alone, would make primary closure a dangerous procedure except in some special cases such as some wounds involving the head, face or chest.

Due to the necessity of extensive débridement without suture, many war wounds require a long period of time for healing to occur unless secondary closure is performed. From the military point of view it is important to secure early healing in order to return the soldier to duty as soon as possible. For the individual, successful secondary closure usually means a better functional and cosmetic result, a more rapid improvement in general condition due to the closure of an open wound, and the avoidance of the possibility of long-protracted ulceration in a large cicatrix. Ulceration may result from lack of blood supply to the central area of such a cicatrix left to heal by second intention.

In a preliminary communication we reported in detail our experience with a group of 138 secondary closures.² Since this report was written our experience has been more extensive with cases of this type, and we have also had an opportunity of seeing more cases relatively soon after the receipt of the initial injury. Overseas military hospitals are employing delayed closure successfully on a very extensive scale, as shown by the recent reports of Kirtley and Trabue,³ Rusbridge, Krajcski and Silver,⁴ and others.

Types of Wounds Suitable for Secondary Closure—The wounds most suitable for this procedure are those involving soft tissues which have been

adequately débrided within the past ten days, that have not been subjected to frequent changes of dressing, and which appear clinically to be relatively clean. Wounds older than ten days showing slight infection in patients who are fever-free may be prepared for closure by a short period of warm wet dressings. Studies are now being undertaken in certain specially designated installations to determine whether or not successful secondary suture may not be accomplished in certain compound fractures. It is also hoped that with careful use and good judgment, penicillin may extend the use of delayed closure to some other cases where at present it is not believed to be a desirable procedure.

Factors Favoring Successful Secondary Wound Closure—These factors are essentially the same as those of importance in the healing of any wound by first intention. Of greatest importance is a wound which is relatively free from infection. Closure without tension, adequate hemostasis, the avoidance of dead space, and suitable postoperative splinting are the most important local factors favoring successful secondary closure. Attention to systemic factors favoring wound healing are important in these cases because many of the patients may be suffering from anemia as the result of extensive blood loss at the time of injury, the diet may not have been adequate during a prolonged period of combat, and the patient is likely to be greatly fatigued.

A normal red cell count, hemoglobin, plasma protein, and vitamin C level in the blood are all especially important in the proper management of such cases^{5, 6, 7, 8, 9, 10, 11}

Sulfonamides have been employed systemically and locally in some cases. It is fair to state, however, that successful closures are possible in a high percentage of cases without the use of these drugs. In our experience, it seemed that wounds clean enough to close would almost always undergo primary healing without sulfonamides. Whereas, if they appeared insufficiently clean for suture, sulfonamide would not enable a closure to be successfully accomplished. This agrees with the findings reported by Kirtley and Trabue³

Preparation of Wound for Closure—Wounds considered applicable for possible closure were carefully guarded from contamination. They were usually inspected briefly, using mask and instrument technic. The final layer of vaselined gauze covering the wound was usually left in place until the patient was actually in the operating room. Extensive wounds were usually dressed in the operating room. In some cases which did not appear to be clean, a period of warm, wet pressure dressings was used from two to five days prior to suture.

Method of Closure—Experience showed that the optimum method of wound closure varied to some extent with the type of wound. In cases having had an adequate débridement within the previous five to seven days, that are fever-free, and at the first dressing appear to be clean, the method of choice is a simple closure consisting of interrupted sutures either plain or of the vertical mattress variety. Wounds older than ten days usually require a period of wet dressings, and do best when treated in a different manner. Such

wounds are much less pliable, the tissues having become relatively fixed. These wounds are best closed by total or partial excision of the wound. In such instances it is best to remove approximately $\frac{1}{8}$ - to $\frac{1}{4}$ -inch of skin and subcutaneous tissue. The granulating base is also best excised. In our earlier experience it was felt that such treatment in old wounds might break down natural barriers to infection. It is believed that the complete obliteration of dead space accomplished by wound excision in the older cases is an important factor in producing primary union in such cases.

ANALYSIS OF CASES

This report deals with a group of 305 secondary closures performed upon 209 patients. The interval from the time of débridement to the time of closure varied from 4 to 47 days. The size of the wound varied from that of a few centimeters to one wound measuring 30 x 8 x 4 centimeters. The majority of the wounds involved the extremities, however, secondary closures were performed on almost every part of the body.

The time of closure was based upon (a) the time the patient arrived at our hospital from forward installations, and (b) the gross appearance of the wound. In 79 closures, cultures were made prior to operation, however, if the wound appeared to be clean on inspection, operation was usually carried out without further delay. In 73 wounds bacteria were found. In almost every instance the organism grown was the staphylococcus. No streptococci were cultured from these wounds.

Results of Closures—The best results, as mentioned above, were obtained in cases closed within ten days of the primary débridement. Five to seven days would be considered the optimum time. There were 224 closures performed within ten days of the initial debridement. One hundred-ninety closures, or 85 per cent, healed without evidence of infection. In 25 cases, or 11 per cent, there was slight infection necessitating the removal of one or two sutures. It is pointed out that in these cases, however, much time was saved for the patient. In only nine instances, or 4 per cent, of this group, did total breakdown of the wound occur. Thus, all of these closures except the 4 per cent that completely broke down may be said to have been of benefit to the patient.

Among the closures undertaken after a period of ten days, 37 wounds were closed by simple suture, undermining the edges of the wound slightly if necessary for closure without tension.

Thirty-eight per cent healed absolutely *per primam*, in 54 per cent it was necessary to remove one to three sutures because of slight infection, while 8 per cent showed total break down of the wound, and were listed as failures. In 44 cases beyond the ten-day interval that were treated by excision of the wound and suture, 64 per cent healed absolutely *per primam*, in 32 per cent it was necessary to remove from one to four sutures, and in only 4 per cent of the closures did the wound completely break down. In a few of the cases a rubber tissue drain was placed in the wound at the time of closure. As our

SECONDARY SUTURES OF WOUNDS

experience increased fewer wounds were drained and the results seemed to be improved. In wounds involving deep fascia or muscle depths, or in old wounds that previously had shown the presence of an extensive infection, a rubber tissue drain is still felt to act as a safety valve and, if removed at the proper time, causes little trouble. Drains, however, should by no means be used as a routine procedure if primary healing is expected in a high percentage of cases.

Seventy-nine wounds were cultured preoperatively and organisms were grown, usually staphylococci, from 73 wounds. No streptococci were found. It is our feeling that practically all of the wounds contained some bacteria and that only a quantitative difference existed. From a practical standpoint, cultures were of relatively little aid, as the clinical appearance of the wound offered sufficient criteria upon which to base closure of the wound.

Concomitant Secondary Closure and Skin Graft—In some instances where there has been extensive tissue loss complete closure without tension may prove difficult or impossible. In such instances it was found that complete closure was usually best accomplished by covering the remainder of the wound with a split-skin graft at the time of partial closure by secondary suture. This method was found applicable to both early and late closures. In some cases with extensive loss of tissue, when adequate débridement had been performed and the wound had not been dressed, a large split-graft was applied at the first dressing in the operating room, when the extremities of the wound were partially closed by suture. In some other instances, late cases where warm wet pressure dressings were used to prepare the wound for closure, split-grafts were also successfully used to secure closure without tension.

SUMMARY AND CONCLUSIONS

- 1 Successful secondary closure of adequately débrided war wounds can be accomplished safely in a high percentage of cases.
- 2 Closure within a ten-day interval results in a higher percentage of wounds which heal by first intention.
- 3 In old wounds the best results were obtained by wound excision.
- 4 Wounds with extensive loss of tissue may often be closed early by the concomitant use of secondary suture and a split-skin graft.
- 5 The importance of both local and general factors in wound healing is emphasized.
- 6 The conclusions expressed in this report are based on a study of 305 secondary closures.

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REFRIGERATION ANESTHESIA AND EVALUATION OF AMPUTATION SITES BY ARTERIOGRAM

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PHYSICIANS AND SURGEONS today are becoming more familiar with the work done on cooling or refrigerating living tissues, Frederick Allen,¹ Brooks and Duncan² and Temple Fay,³ and their associates, have made the greatest contributions up to the present time. Allen reported his experiments on the tourniqueted limb immersed in ice about five years ago. He discussed the physiology of the ligated limb with reference to preservation of tissue, lowered metabolic requirements and the surgical possibilities available to us under lowered temperatures. Brooks and Duncan made their studies of the effects of temperature on the survival of anemic tissue. Temple Fay reports 100 cases of general refrigeration where the whole body temperature is reduced to around 80° F to 90° F, the lowest temperature obtained was 74° F by rectum and the longest period of refrigeration was eight days.

This discussion will be limited to the use of lowered temperatures for the purpose of limb amputations. In the Montreal General Hospital the procedure was carried out on 22 patients. The cases referred to were in nearly every instance grave operative risks, some of them would not have been offered the help of surgery if it were not for this method of anesthesia. For example, there is the severely injured who is already in shock, or the diabetic arteriosclerotic, and the cardiorenal deficiency case, then there is the senile decrepit type who through malnutrition or chronic disease would not weather a standard type of operative procedure under general or spinal anesthesia.

FATALITIES

As there are four deaths in this small series it may be instructive to go into some detail with each fatality.

Case 1—A male, age 56, was brought in by ambulance, suffering from a fractured skull and a compound fracture of the left femur. The soft tissue injury at the site of the fractured femur was extensive and involved tearing of muscle sheaths and mangling of the muscle fibers. For the first three days he was treated for shock, and during this time the injured limb was splinted and a thorough debridement of the wound was carried out, followed by a sulfathiazole emulsion pack. On the fourth day the temperature rose to 103° F. The limb became dark in color, although the popliteal pulsation was still palpable. There was a foul odor from the wound, and the general picture was one of septic absorption. It was felt that a high amputation was the only hope of saving his life. This was undertaken under refrigeration. He died the next day. Postmortem showed *Cl welchii* in the thigh muscles.

Case 2—A female, age 80, suffering from arteriosclerosis. She had hypertension, a rough systolic murmur, and the heart grossly enlarged to the left. There was ankle edema and shortness of breath. On the right heel was a dark reddish patch and from

that area was a gangrenous process spreading over the foot. Amputation seven inches below the knee joint was carried out under refrigeration. For some unaccountable reason in this case the ice pack contained salt and the surface temperature was reduced to the freezing point. When the leg was lifted out of the ice in the operating room there were blebs on the skin surface due to the excessive low temperature. These were aspirated and on culturing were shown to contain *C. welchii*. She was treated at once by every means in her defense but died of gas gangrene seven days later.

Case 3—An elderly woman of uncertain age. She also had arteriosclerosis and diabetes with gangrene of the left leg. An ice pack was instituted in the usual way and a mid thigh amputation carried out without any apparent ill effects. She died of a cerebral hemorrhage a few hours after operation.

Case 4—Female, age 57. An arteriosclerotic diabetic, almost blind. She had been admitted several times previously for an unhealed ulcer on the right heel. On the present occasion, there was evidence of a spreading gangrene over the foot and ankle. The dorsalis pedis artery and the peroneal artery were pulseless. The popliteal artery was, on the other hand, quite normal. An amputation at the site of election was carried out under refrigeration. She died of a rapidly progressing gas infection on the fourth postoperative day.

COMMENT—Since three of the deaths were due to gas gangrene we have naturally been very disturbed. The first case with the deep muscle wound fell in line very well with our knowledge and experience of gas infections. The second case, however, had no open wound until the blebs were formed by the unfortunate excessive low temperature caused by the salted ice. We then feared that we were introducing the organism through the medium of river ice and henceforward decided to use artificial ice or mechanical refrigeration entirely. The fourth case died of gas gangrene in spite of the precautions prompted by the previous experience and improved technic. The only open wound was a chronic gangrenous ulcer surrounded by inflammatory tissue. There was, however, thick, dark colored leathery skin about the ulcer and covering a tough, ligneous deep tissue surrounding the lymphatics. Gas-forming organisms have been isolated on numerous occasions from devitalized tissue in the region of chronic ulcers. We are of the opinion that the spores may lie dormant in the lymphatics and also in the deep tissues surrounding the lymphatics. It is probable, too, that tissues so affected may extend high up in the limb.

GENERAL PROCEDURES

Refrigeration anesthesia cools and numbs the tissue cells *en masse*. It is, therefore, a general tissue depressant without any particular selective action on nerve trunks. Refrigeration produces first of all a vasoconstriction and later a vasodilatation, this reduces edema and minimizes transudation of tissue fluids rendering the tissues firm. Shortly after refrigeration commences there is a mild analgesia over the once painful extremity. The patient, relieved of his agonizing pain, may now enjoy a substantial meal before going to the operating room or immediately afterward. There is no shock to the procedure whatsoever, as determined by the ordinary signs and symptoms or by the Scudder estimation. There is no real necessity of a sedative although in many nervous people it is probably advisable. The anesthesia is

TABLE I

Hosp No	Date	Sex	Age	Reason for Amputation	Site	Material used	Drainage	Result
1937	Apr 11/42	F	56	Diabetic gangrene	6" below knee	C G & Dermol	No	Primary healing
2394	Apr 20/42	M	49	Severe injury	Upper third thigh	C G & Dermol	Yes	Died
2909	May 12/42	M	70	Art scl gangrene	6" below knee	C G & Dermol	No	Primary healing
2150	July 2/42	M	29	Severe injury	Mid calf	Chr c g & s w g	No	Secondary repair
4866	Aug 26/42	M	75	Art scl gangrene	6" below knee	Chr c g & s w g	No	Primary healing
2686	Aug 27/42	M	64	Lues—gangrene	Mid thigh	Chr c g & s w g	No	Primary healing
5428	Aug 31/42	F	62	Diab gangrene	6" below knee	Chr c g & s w g	No	Primary healing
5781	Sept 21/42	M	26	Ca right foot	6" below knee	Chr c g & s w g	No	Primary healing
6121	Sept 30/42	M	61	Diab gangrene	6" below knee	Catgut & s w g	No	Primary healing
8189	June 6/43	M	38	Severe injury	6" below knee	Catgut & s w g	No	Secondary repair
8283	Feb 22/43	F	65	Diab gangrene	Lower third thigh	Silk & Dermol	No	Primary healing
2175	Apr 15/43	M	38	Severe injury	Lower third forearm	Chr c g & silk	No	Primary healing
2463	June 21/43	F	80	Art scl gangrene	6" below knee	Chr c g & silk	No	Died
2801	June 24/43	M	75	Art scl & abscess	Amp hand	Chr c g & silk	Yes	Primary healing
5780	Sept 20/43	M	77	Art scl gangrene	Mid thigh	Chr c g & silk	Yes	Delayed healing
5834	Aug 21/43	M	65	Embolism popliteal	Mid thigh	Chr c g & silk	Yes	Delayed healing
6458	Oct 14/43	M	76	Diab gangrene	Mid thigh	Chr c g & silk	Yes	Died
7134	Nov 20/43	M	51	Diab gangrene	6" below knee	Chr c g & silk	Yes	Died
316	Jan 21/44	F	58	Diab gangrene	6" below knee	Chr c g & silk	Yes	Delayed healing
856	Mar 20/44	F	60	Diab gangrene	6" below knee	Chr c g & silk	No	Delayed healing
391	Mar 31/44	F	71	Diab gangrene	Mid thigh	Chr c g & silk	Yes	Primary healing
1543	Apr 15/44	M	74	Emb popliteal	Upper third thigh	Chr c g & silk	No	Secondary suture

c g =catgut, Chr c g =Chromic catgut, Art Scl =Arteriosclerotic

adequate and will last about one hour, thus allowing the surgeon to carry out any type of amputation procedure he desires. The sawing of the bone sometimes disturbs the patient but he will generally admit there is no pain. Severing of the large nerve trunks is quite painless but one cannot pull the nerve down from a higher cut without some pain, to obviate this discomfort it is quite easy to separate the muscle fibers upwards an inch or so and in that way cut off the nerve above the line of amputation. Or, if the surgeon desires, he may inject novocaine into the nerve, or novocaine and alcohol, to avoid the painful neuroma later. This brings up the question of the tourniquet, and perhaps suggests its only value. In a completely ligated limb the large nerve trunks are absolutely senseless to pain, whereas in the nonligated limb the analgesia is sufficient to handle the nerve without undue discomfort.

TOURNIQUET

Allen, and his coworkers, have proved to their own satisfaction that the tourniquet is harmless under reduced temperatures. Others have remarked that the dangers of the tourniquet are reduced but not entirely eliminated. Gerald Pratt⁴ stated that "Ice is reserved for those patients whose chances of surviving a general anesthetic are very poor and where the dangers of the tourniquet are less than the dangers of anesthesia." In the small series at the Montreal General Hospital the tourniquet was dispensed with in 18 of the 22 cases. This was done, realizing fully that warm blood was surging through the depth of the limb to be chilled. The only precaution was to chill the limb long enough and high enough, an average of four hours for the upper third of the tibia and five hours for thigh amputations. It is now common knowledge that the limb can be immersed in ice for days, as long as there is no tourniquet. We have attributed the early and uneventful healing of the stump wounds to the fact that the tourniquet was not used in these cases. It must be borne in mind that the tissues dealt with here are already devitalized and the trauma of the scalpel alone may be more than the local healing processes can deal with. The tourniquet, we believe, weighs heavily against early healing by adding further trauma through local pressure on unfavorable tissue material which is traversed by sclerosed capillaries to the wound edges.

TECHNIC OF APPLICATION

The technic used is a modification of that described by Allen. Usually a mild sedative is given before immersion of the limb into the ice. We have used $\frac{1}{6}$ gr morphine sulfate and $\frac{1}{100}$ gr hyoscine. The refrigerating apparatus is made up by materials which are available in any ward. First, an ordinary single leg cradle is inverted in the bed and lined with a rubber sheet sufficiently long to extend from the ischial tuberosity downwards to beyond the foot of the bed and into a pail on the floor. Finely chopped artificial ice is then distributed about four inches in depth along the floor of the



FIG 1

FIG 2

FIG 1—Produced by injecting 20 cc 70 per cent diodrast into the femoral artery just below the inguinal ligament. Showing patency of femoral artery and popliteal artery, with its bifurcation into the anterior and posterior tibial arteries. Some cases show a very much better geniculate anastomosis.

FIG 2—Arteriogram of Case No 5834. Produced by injecting 15 cc diodrast into the femoral artery just beneath the inguinal ligament.

Note the absence of continuity of the lower part of the femoral artery and the upper part of the popliteal, with filling of the popliteal through anastomotic network, which, although patent, is insufficient for maintenance of the lower leg.

trough from the ischial tuberosity to beyond the foot of the patient. The limb is then placed upon the four-inch mattress of ice. Sufficient ice is then added to bury completely the member including the toes. The head of the bed is elevated enough to allow adequate drainage of the melting ice down the rubber trough into the pail on the floor. This drainage is important to obtain a constant temperature and prevent maceration of the skin. The ice should be replenished frequently to compensate for melting and settling. The temperature thus obtained at the skin surface is about 5° C. If a tourniquet is to be used it is applied one hour after refrigeration.

commences During refrigeration the patient may be given coffee or whisky or a regular meal The duration of ice pack with the tourniquet is about two hours for ankle, three hours for the upper tibia, and four hours for thigh amputations Without the tourniquet the refrigeration required is about one hour more at each site but it may go on indefinitely without harm When the patient is brought to the operating room the surgeon and his assistant must be scrubbed and prepared to operate The patient is lifted out of the ice pack and the leg prepared with ether, alcohol and iodine Note that this is the only skin preparation the limb has been given The lower part of the extremity is bandaged and the draping completed It is preferable to use cold saline and cold instruments but the operating room is kept at the regular temperature The amputation procedure is carried out with leisure, and the wound usually closed without drainage A compression dressing is applied to the stump and the patient returned to the ward with three ice bags over the dressing One ice bag is removed every 24 hours

AMPUTATION SITE

The amputation site is undoubtedly going farther down the limb This is attributed not only to refrigeration without tourniquet and improved metabolic condition of tissues, but also to the use of arteriograms Ice anesthesia enables the surgeon to reamputate without undue risk, but if an arteriogram is available and the proper site ascertained it is a sounder procedure Very often there is a wide and adequate collateral circulation, allowing a low amputation site, on the other hand the surgeon may believe he is feeling a pulse in the popliteal space when actually the impulse is being transmitted through five inches or more of blood clot

The color plate, consisting of six individual cuts, has been arranged to show the salient features in connection with refrigeration anesthesia, according to the Montreal General Hospital technic, omitting the use of a tourniquet

The case is one of a diabetic, who had been bedridden for three to four years on account of recurrent ulceration and cellulitis of the right foot, ultimately rendering the lower leg and foot a constant source of infection, pain and irritant to the diabetic condition

The lower leg and foot shows deformity, blanching and pigmentation, before emersion in the ice pack (Fig 1)

The cradle is improvised as a structural support for a rubber sheet, forming a trough, which extends approximately to the ischial tuberosity and distally is extended as a spout for drainage into a pail Four inches of finely chopped ice (snow) is placed at the bottom of the trough, the limb is then placed on the bed of ice and entirely covered with ice, including the great toe A thermometer is placed in the ice and the head of the bed is elevated about one foot to give adequate drainage As you will see, the patient appears comfortable and rested (Fig 2)

After a minimum period of four and one half to five hours, the patient is wheeled to the operating room on her bed, with ice pack *in situ* The lower end of the trough is opened by relaxing the paper clips and the ice is disposed of by emptying into a pail (Fig 3)

The patient is rapidly transferred from the bed to the operating table The limb is dried with a sterile towel You will notice that the lower leg shows a very definite erythema when compared with Figure 1 a typical finding when satisfactory refrigeration anesthesia has been attained The limb is then rapidly prepared with ether, alcohol, and iodine This, incidentally, is the first skin preparation and the only one We do not shave (Fig 4)

The limb is draped with all the staff on hand The amputation is carried out in the routine manner according to classical amputations There is no need to hurry, as the skin is divided it retracts very little The tissues are firm and easily handled The muscles retract slightly, do not twitch, and are easily cut, and the bleeding is minimum On sawing the bone, some of the patients have a sensation as if having a tooth drilled There is no pain on ligation of the vessels Injection of novocaine and alcohol prior to division of the nerve is advisable but not necessary (Fig 5)

Bleeding points are ligated with 'C' silk The vessels ligated with No 2 silk The wound is closed without drainage, utilizing subcutaneous sutures with 'C' silk, and skin apposition with vertical mattress sutures of No 2 silk (Fig 6)

Upon completion of amputation, a pressure dressing is applied, consisting first of gauze, then absorbent held in position by a gauze bandage which has been soaked in water The gauze bandage when soaked, dries and shrinks, giving adequate pressure This is reinforced by a sterile plumber's waste dressing, held in position by a flannel bandage No attempt is made to use any other form of splinting These dressings are not disturbed for a period of ten days unless there is a smell of stale urine, which is, in our opinion the first indication of gas infection



1



2



3



4



5



6

Arteriography is a comparatively new field but will undoubtedly offer a great contribution in establishing for us the proper site for amputation and go hand in hand with refrigeration in the conservation of limb length and lives. Our experimental work in arteriography has rendered us many interesting determinations with regard to the collateral circulation which we have been unable to ascertain by skin temperatures or oscillometric readings. Furthermore, arteriography determines the exact patency of the main vessel at a higher level than we would anticipate by any other tests. In other words, arteriography eliminates any element of doubt as to the site of amputation. We hope, in a subsequent report on amputations with refrigeration, to submit a detailed account of the value and technic of arteriography.

CONCLUSIONS

We have given our experiences in the use of refrigeration for amputation of limbs and also detailed the technic which we generally use. We have enumerated and discussed the fatalities. The mortality rate was higher than in most series of amputations, but the explanation is clear when one considers the cases offered for this method. The incidence of shock was absent in every case. The percentage of gas bacillus infections has been dealt with and is undergoing further study. The general feeling is that the organism lies dormant in the devitalized tissues. The tourniquet has been largely dispensed with in this series. A preliminary discussion on arteriography was included.

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THE BIOPSY AS AN ACCURATE GUIDE TO THE DECISION OF EARLY SKIN GRAFTING

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WHEN A BURN WOUND requires skin grafting, it is desirable that it be done as early as possible

The reasons for early skin grafting are

- 1 To obtain skin coverage as soon as possible in order to prevent disability or loss of life from infection or wasting
- 2 To restore the skin surface to a good functional condition
- 3 To allow for earliest movement of joints, tendons and muscles
- 4 To prevent deformities
- 5 For practical economy

It is important then to have some means of determining whether the wound can be expected to heal spontaneously and satisfactorily, or whether it cannot be expected to heal spontaneously and satisfactorily, and should be skin grafted

Immediately after the accident, when the patient first comes under observation, it is impossible to be certain to what depth the damage has extended. Even by biopsy, at this stage, the depth of destruction cannot be accurately determined, because heat of an intensity insufficient to cause charring may coagulate and fix the tissue well enough to make it impossible to distinguish between viable and nonviable tissue. Anyway, the assessment of the depth of a burn just after the accident is not important, as primary skin grafting is not practicable except when the burned area is very small. Besides, the condition of the patient usually precludes any surgical procedures of any magnitude other than proper dressings.

Time will reveal, by the reaction of the wound, the true depth of the burn, provided infection is controlled. It will either show sufficiently advanced re-epithelization in the third week, or granulation tissue will appear with no or inadequate epithelization.

This latter state of affairs we believe should not be allowed to go on, because granulation tissue organizes into fibrous tissue, and the longer it grows the more fibrous tissue will be laid down. Even if re-epithelization should occur later, the newly formed epidermis will have an underlay of fibrous tissue instead of fibro-elastic corium, *i e*, scar skin will form and may prove very unsatisfactory. Indeed, it later may have to be removed and replaced by a skin graft.

At The Montreal General Hospital, the method of treatment used by the burn team,¹ on the Surgical Service of Dr Fraser B Gurd, includes the infrequent occlusive compression dressing with an emulsion of sulfathiazol in

an oil-in-water base This dressing, except in obviously very superficial burns which require no grafting, and heal within one week, is sometimes removed as early as the ninth day More commonly, however, it is removed about the thirteenth or fourteenth day, with the intention of grafting if necessary, because it is considered that this is the most desirable time to graft, if at all possible Wound excision may be required This includes the removal of slough and granulation tissue, if any be present, and even scattered islands of epidermis But it is by no means easy, even at this stage, to be certain from the gross appearance of the wound, whether it is healing satisfactorily or whether it cannot heal satisfactorily, and will require grafting Even the most experienced surgeon is prone to err in this matter The presence on the surface of the wound, of a thin coagulum of exudate masks the true nature of the wound surface

The study, in the Department of Pathology, over a period of four years, of numerous blocks of tissue, submitted by the burn team from burns in various stages has taught us much about the pathology of burned skin, how it heals and how it may be expected to heal A direct outcome of this study was the decision, about a year ago, to submit at the time of removal of the first dressing, all questionable cases to biopsy, in order to determine the expectancy of the healing of the wound It soon became the practice to prepare rapid frozen sections of this tissue at the operating room, and upon the report of the pathologist, the decision to graft or not to graft is made at once These specimens should be at least 5 Mm wide to allow for proper handling

As was pointed out in a previous report,² the healing of a burn depends upon the viable epithelium, in the burned area, available as sources of reepidermization These sources are the epidermis at the margins of the wound, surface epithelium that has escaped destruction, hair follicles, sebaceous glands and sweat glands

It was further pointed out that for satisfactory spontaneous healing, there is required at least a sufficient number of hair follicles and sweat glands so that hair follicles, which lie, except in hairy parts, at a higher level than sweat glands, must be spared in sufficient numbers, if spontaneous satisfactory healing is to be obtained This applies to the donor site as well as to the burn wound

If destruction should involve most or all of the hair follicles, but spare the sweat glands which lie at a deeper level, spontaneous reepidermization may still be expected, but the process will be slow and it will be attended by the formation of granulation tissue which organizes into fibrous tissue, so that the remains of the viable deep layer of the fibro-elastic corium becomes overlaid by a thick layer of scar tissue covered by hyperkeratotic epidermis—an unsatisfactory result

If the destruction extends deep enough to involve the sweat glands, there will be no sources of reepidermization other than that at the margins of the wound, and this, in all but very small burned areas, is inadequate

In doing the biopsies, the finding of destruction of the skin to a level below the hair follicles indicates that satisfactory spontaneous healing cannot be expected, and that skin grafting is required

On the other hand, if there are viable hair follicles present, spontaneous satisfactory healing can be expected. Usually, at this stage, if viable follicles are present, reepithelization from them and from sweat gland ducts will have already become established if not completed

The reader may here be reminded that, since the superficial sources of epidermal regeneration either in a burn or donor site, are of the utmost importance, they must be spared and not further damaged by too vigorous handling, by the application of escharotics, by infection, by improper dressings, or by the too early and too frequent changing of dressings

The method^{1, 2} used by the burn team in this hospital of dressing these wounds has successfully provided for all these requirements. Besides the bacteriostatic sulfathiazol emulsion, the wide-meshed gauze and the infrequently changed compression dressing immobilizes the dressing on the wound surface and thereby prevents slipping of the dressing, and rubbing off of the delicate regenerating epidermis, and it excludes contamination by pathogenic organisms

The following selected case reports will illustrate the usefulness of the biopsy for guiding the surgeon in the procedure of early skin grafting

SELECTED CASE REPORTS

Case 1—A male, age 20, suffered a flame burn on the medial posterior aspect of the right thigh, on April 3, 1944. He was admitted to The Montreal General Hospital about one hour later. A compression dressing with sulfathiazol emulsion was applied.

The dressing was removed on the twelfth day, and as there was some doubt as to the status of the wound, a biopsy was done and the wound was redressed. Paraffin sections (Fig 1), showed well advanced reepithelization. Hair follicles, sebaceous glands and sweat glands were intact. There was some edema and cellular infiltration just beneath the epidermis, and about the hair follicles. Elastic tissue stains showed elastica right up to the epidermis.

Interpretation Well advanced, satisfactory spontaneous healing of a superficial burn.

Four days later, on the nineteenth day, the second dressing was removed. Complete reepithelization was then obvious. No further dressing was needed, and the patient was discharged from hospital on the nineteenth day.

Case 2—A male, age 49, sustained a burn of the face and right forearm by burning fat, on December 22, 1943. He was admitted to hospital six hours later. A compression dressing with sulfathiazol emulsion was applied.

The dressing was removed on the thirteenth day. The opinion of the majority of the surgeons present was that grafting was obligatory. A biopsy was done and a graft was then applied.

A few days later, a paraffin section (Fig 2) of the biopsy showed quite well advanced reepithelization, but still patchy with unhealed areas. The interpretation was that spontaneous satisfactory healing could be expected. The result was that when the second dressing was removed, fourteen days later, the graft was found to have taken on the small nonhealed areas, but had been lifted up by spontaneous re-

epidermization in the areas of lesser burn depth. A biopsy at this time (Fig 3) shows the graft separated from the reepidermized wound by a layer of epidermis and desquamated keratin. Wound excision with removal of the graft and healing wound surface was followed by the application of another graft, which took well.

COMMENT—It is felt that this wound would have healed well spontaneously and without grafting at all.

This patient was in hospital for a total of 44 days, but might have been discharged much earlier had the wound been allowed to heal spontaneously.

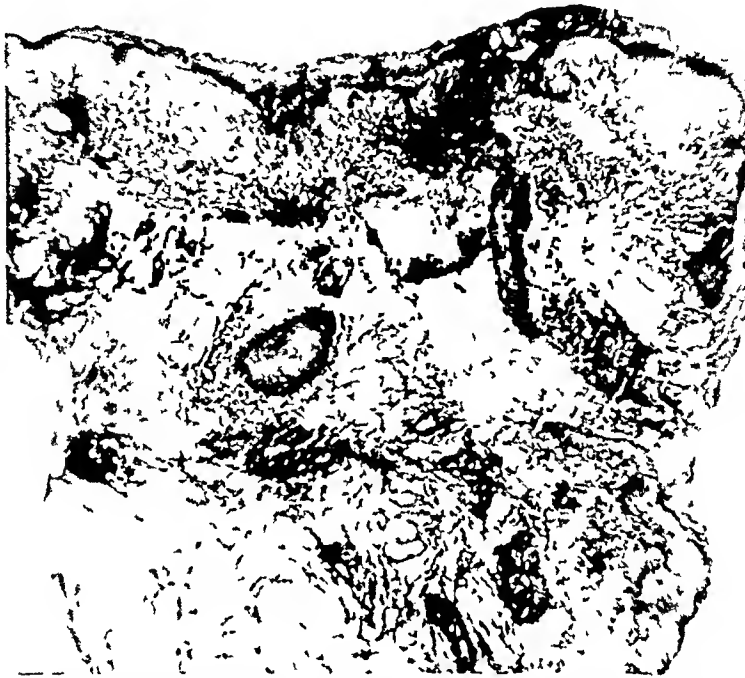


FIG 1—Case 1. Biopsy, 12th day. Reepidermization is complete. There is a viable hair follicle in the centre of the field and part of one at the lower right margin.

There is moderate inflammatory cell infiltration and edema still present in the corium. On the surface there is a thin layer of coagulated exudate.

The experience with these two cases led to the practice of not proceeding with the graft at this early stage without confirmatory histologic evidence of the status of the wound, which can be obtained by biopsies, and at once by quick frozen sections.

Case 3—A male child, three years old, sustained a 30 to 35 per cent hot water burn involving the right side of the trunk, right arm, right leg and part of the left leg and the right hand. The wound was dressed as usual.

On removal of the first dressing on the fourteenth day, there was complete healing of all parts, except for a 5- x 3.5-inch area in the midpart of the right side of the chest. Several experienced surgeons, including visitors, said that grafting was not necessary. A biopsy was done and the area was redressed.

Paraffin sections (Fig 4) revealed a deep burn in which there were no recognizable follicles or sweat glands, and no evidence of reepidermization. There was intense inflammatory cell infiltration throughout the corium and in the subjacent fat.

The interpretation was "deep burn" with no possible sources of reepidermization.

FIG 2

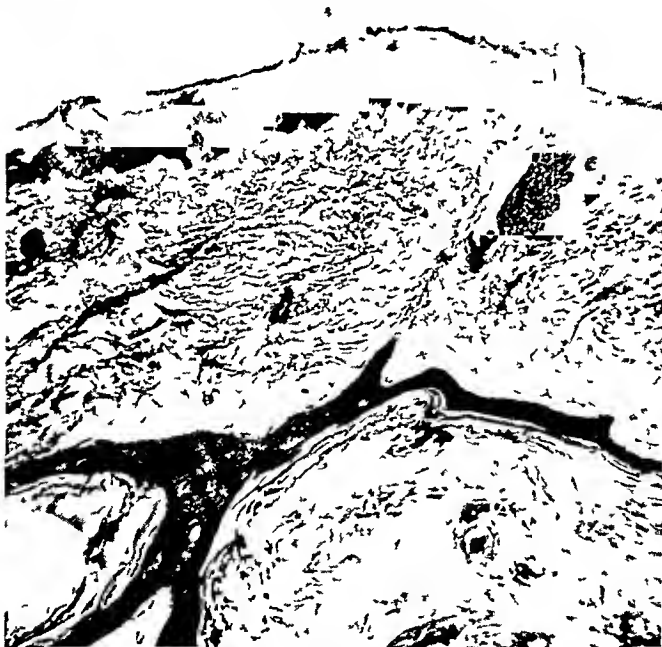


FIG 3

FIG 2—Case 2 Biopsy, 13th day. There are viable hair follicles and sweat gland ducts from which reepidermization had spread over most of the surface.

There is also marked inflammatory cell infiltration and slight edema of the corium.

The bar along the lower margin of the section is fresh blood clot.

FIG 3—Case 2 Biopsy, 27th day, 14 days after grafting. Note the spontaneously regenerated epidermis under the graft separating it from the healing wound.

BIOPSY AS GUIDE FOR SKIN GRAFTING

Removal of the dressing was unnecessarily delayed until the twenty-fifth day, and a graft was applied. The patient was ready to be sent home on the thirty-seventh day, but was retained in hospital until the forty-fifth day for other reasons.

FIG 4

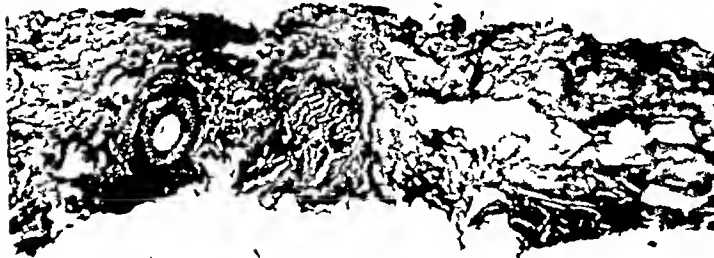
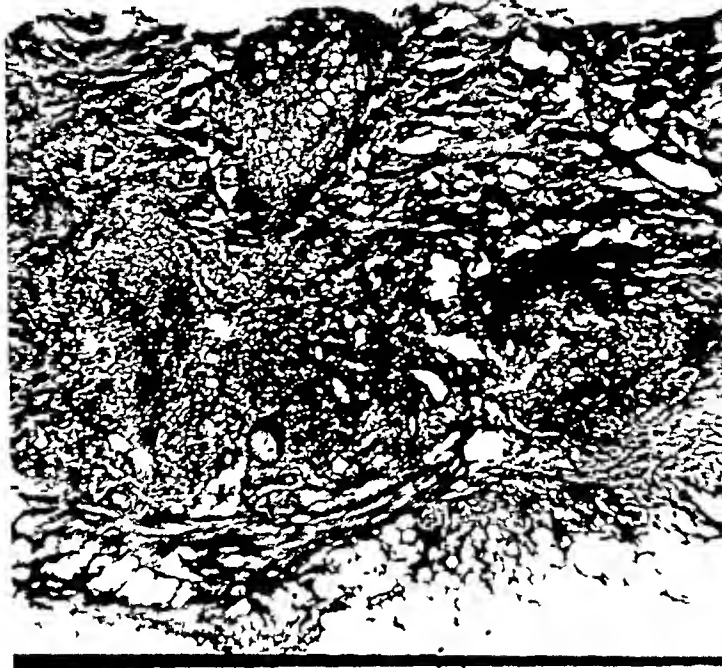


FIG 5

FIG 4—Case 3. Biopsy, 14th day. There are no surface epithelium, hair follicles, or sweat glands recognizable. There is intense inflammatory cell infiltration which extends into the subcutaneous fat. Destruction has extended to practically the full depth of the skin. Spontaneous healing could not be expected.

FIG 5—Case 4. Biopsy, 9th day, paraffin section. To the left is a viable hair follicle, but to the right there are no follicles or sweat glands. In the rapid frozen sections there was regenerated surface epithelium only over the end containing hair follicles. This was lost in the handling of the biopsy in the preparation of the frozen sections.

Case 4—A male, age 38, received a flash burn of the face and upper extremities on the day of admission, June 19, 1944. The wound was covered by a compression sulfathiazol dressing. On the ninth day healing was found complete, except for an area of 3 x 4 inches just above the elbow on the extensor surface.

A biopsy was done in a radial axis at the periphery of the wound. The frozen section showed hair follicles and reepidermization at the outer end, but in the remainder of the section, destruction had extended down to the sweat glands.

A graft was then applied over the whole area, with a good take, except at the periphery where spontaneous healing occurred. The patient was discharged on the twenty-ninth day.

Later paraffin sections (Fig 5), show the deep destruction at one end and a viable hair follicle at the other. The surface epithelium seen here in the frozen sections, is not present in the paraffin sections. In the deeply destroyed area, there is inflammatory cell infiltration in the remains of the corium, and along the subjacent margin of the subcutaneous fat.

The interpretation of this biopsy is that marginal healing was in progress.

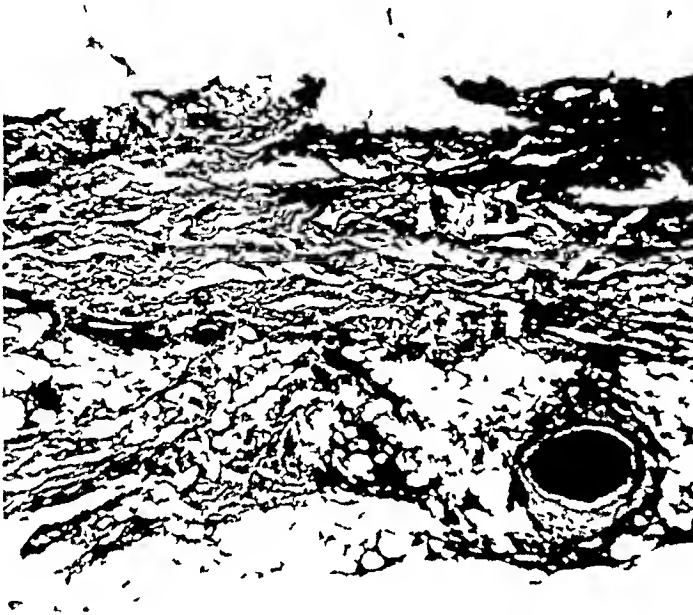


FIG 6—Case 6 Biopsy, 13th day. Only a strip of the base of the corium remains and there are no follicles or sweat glands. There is moderate inflammatory cell infiltration in the subcutaneous fat.

Note the artery plugged with coagulated blood.

but beyond this satisfactory spontaneous healing could not be expected, and that grafting should be carried out.

Case 5—An adult male, age 44. On admission there was a seven-day-old 4- x 5-inch steam-jet, infected burn over the right deltoid region. A compression sulfathiazol dressing was applied, and four days later (eleventh day), it was taken down.

A biopsy by frozen sections revealed a deep burn with no sources of reepithermization. A graft was applied. The patient was discharged on the seventeenth day.

Case 6—A male, age 47, sustained a burn by molten steel on the face, left wrist and right foot, which was treated by compression dressing and sulfathiazol emulsion. On the thirteenth day the dressings were removed, and healing was found complete except for a 3- x 4-inch area on the dorsolateral aspect of the right foot. The status of this wound was doubtful.

Biopsies by frozen sections (later confirmed by paraffin sections [Fig 6]), revealed a deep burn with no sources of epithelium available for reepithermization.

The wound was excised down to a satisfactory level, and a graft was applied. The dressing was removed on the twenty-sixth day when there was a 100 per cent take of the graft. The patient could have been discharged on the twenty-eighth day, but was held until the thirty-eighth day for investigation of neurosyphilis.

SUMMARY

The desirability of the use of biopsies in the management of early skin grafting of burns is discussed and six selected cases are cited as illustrations. All these wounds were undressed between the ninth and fourteenth day with the intention of grafting if necessary. Biopsies were done on all six cases because of doubt as to the status of the wounds. In the first three cases delayed paraffin sections were used, and in the last three, rapid frozen sections and delayed paraffin sections were employed. In Case 1, the biopsy showed well-advanced healing and no grafting was needed. In Case 2, the biopsy and grafting were done at the same time. Later, the examination of the biopsy indicated that grafting was not needed and this was borne out by the subsequent behavior of the graft. In Case 3, after biopsy on the fourteenth day, the wound was redressed to await the report on the paraffin sections. This indicated the necessity of grafting, which was not done until the twenty-fifth day—an unnecessary delay. Had a frozen section been made, grafting might have been done on the fourteenth day. In Cases 4, 5 and 6, rapid frozen section biopsies at the time of removing the first dressing on the eighth, eleventh and thirteenth day, respectively, all indicated the necessity of grafting, which was carried out without further delay, and with entirely satisfactory results.

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SKIN GRAFT OF DORSUM OF HAND

USE OF LARGE SIZE DERMATOME* TO OBTAIN ONE-PIECE PATTERN

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EXTENSIVE WAR BURNS of the hand involving the deeper layers of the dermis and the full-thickness of the skin have required total replacement of the skin of the dorsum by skin grafts of intermediate thickness. In such cases, a considerable area of skin graft is required to restore normal flexion and function of the hand and fingers. At least two pieces of skin graft usually are needed when the graft is cut free-hand and often when it is cut with Padgett's dermatome. It is not infrequent to see the junction scar-line between the graft become hypertrophic or even cheloidal, such scars not only are unaesthetic but also may impair the function of the hand. It became apparent, therefore, that the use of a large one-piece skin graft accurately cut and fitted according to a pattern was desirable. A large drum (Fig 1) which could be fitted over the ordinary Padgett dermatome was constructed. With this drum a piece of skin graft covering the area of the drum (8 x 6 inches) may be removed when cut transversely across the thigh. After the dorsal scar of the hand and fingers has been completely excised, a pattern of the resulting defect is made, the hand being maintained by a splint in a position which is close to the position of function, but which permits the application of the largest piece of skin graft with the fingers and wrist in semiflexion (Fig 2). This pattern is then reversed and applied to the raw surface of the skin graft on the drum (Fig 3). A pattern graft is cut by incising the skin graft on the drum with a scalpel, following the contour of the pattern. The skin graft is removed from the drum, while this procedure is being done, fine sulfanilamide powder is rubbed over its cemented surface to neutralize the cement, and prevent the adhesion of the graft to itself. The skin graft is applied to the raw area, fixed by a few interrupted sutures and its edges are sutured to the edges of the defect by a continuous running suture of fine silk. A pressure dressing is then applied over the skin graft in the usual manner with cotton or mechanics waste.

* The large drum shown in Figure 1 was made two years ago for the author by Thackeray & Sons, London, England

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SKIN GRAFT OF DORSUM OF HAND

FIG 1A

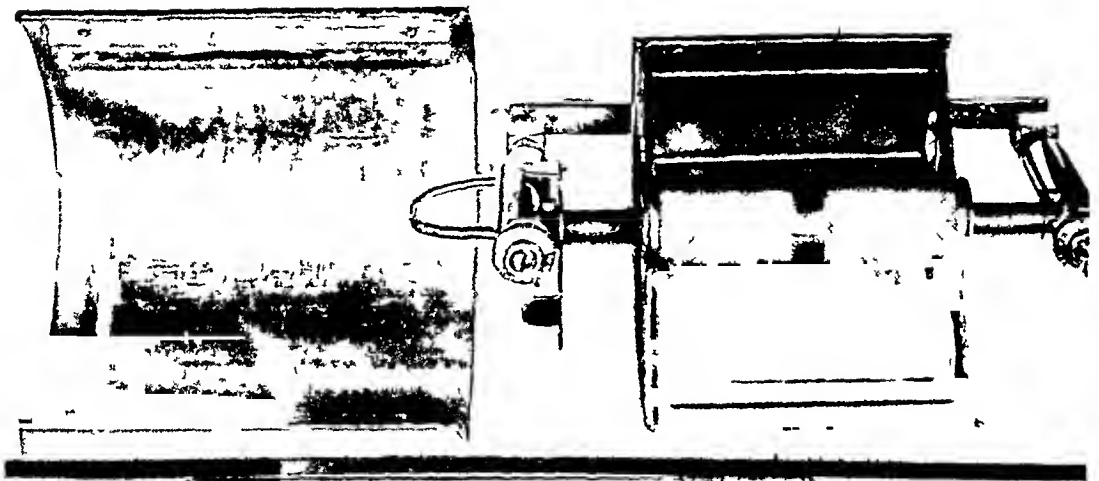


FIG 1B

FIG 1A—On the left is shown the large drum (8 × 6 inches) which is made to fit accurately over the drum of Padgett's dermatome (on the right)

FIG 1B—The large drum has been fitted over the drum of Padgett's dermatome to which it is held by a spring clamp (Note Small dots on photograph indicate this spring clamp)

FIG 2



FIG 3

FIG 2—Dorsum of the hand after the excision of all of the cutaneous and subcutaneous scar. The hand is immobilized in this position by a splint. A pattern is made of the defect which extends around the radial aspect of the thumb and around the ulnar border of the hand.

FIG 3—The pattern of the defect is reversed and applied to the raw surface of the skin graft on the drum. A one piece pattern skin graft may now be cut by incising the graft around the pattern. The excised scar is shown below the drum. (Note: This is the scar tissue excised from the hand—not the graft.)

PROXIMAL LIGATION AND THROMBECTOMY FOR PHLEBOTHROMBOSIS OF THE FEMORAL AND ILIAC VEINS*

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THE TREATMENT OF PHLEBOTHROMBOSIS by thrombectomy is not an unchallenged procedure. There are many who feel that if the patient is properly treated with anticoagulants operation is unnecessary. By thrombectomy I mean the removal of the clot from the iliac vein as it extends above the inguinal ligament. Even among surgeons there is a more radical group who believe in proximal ligation even if the vena cava itself has to be ligated. All methods of therapy are directed toward eliminating pulmonary embolism.

May I state that I believe more lives will be saved by thrombectomy than by the use of anticoagulants alone. The literature in recent years has brought forward advocates of the thrombectomy treatment. Fine, Homans, Arthur Allen, and his group, are all advocates of this procedure. While I have had only a limited experience, nevertheless, I believe a careful analysis of this small series may prove of value. In presenting this subject I wish to discuss briefly the pathology, in order that we understand the limitations of this discussion.

In the long veins of the extremities there are two processes that occur largely postoperative. These two processes are usually clear-cut, but they sometimes merge one into the other. These processes are thrombophlebitis and phlebothrombosis.

Thrombophlebitis, as the name indicates, is a phlebitis and periphlebitis associated by sometimes an absence of a clot in the lumen. It is usually initiated with a chill, high temperature, swelling of the leg, marked tenderness, and often redness over the course of the involved vein. It is characterized very largely by perilymphatic involvement, as well as involvement of the walls of the vein. Embolism following thrombophlebitis is relatively rare. It occurred in 10 per cent of the Toronto series and about 12 per cent of the series analyzed by the Mayo Clinic.

Phlebothrombosis is characterized by a blood clot which fills the lumen of the vessel. The onset may be sudden. It is not accompanied, as a rule, with as high elevation of temperature or with as great swelling of the leg as in thrombophlebitis. Homans has shown experimentally that if one wishes to create a so-called *alba dolens* in experimental animals it is necessary to destroy the lymphatics. Mere ligation of the vein will not, as a rule, create swelling.

In this presentation I wish to discuss the latter of the above two subjects and discuss it largely as a means of preventing the formation of pulmonary

* Read before the Philadelphia Academy of Surgery, November 6, 1944

embolism, for it is in this type that emboli are more frequent. Symptoms may be silent and not recognized until after the embolus has separated. I wish also to discuss the two methods of operative procedures, *viz* Proximal ligation, and (2) thrombectomy.

Proximal Ligation—This is performed when the clot in the vein has not extended upward as far as the inguinal ligament. This is of course a safe procedure and one which, in my opinion, should be undertaken much more often than it is. The patient can then be immediately mobilized without fear.

Thrombectomy—When the thrombus has extended beyond the iliac ligament, thrombectomy may be performed by mechanical removal, such as using thin, narrow forceps for extraction, or by suction. I wish to concentrate on the latter procedure, and to analyze a series of cases I personally have had, and give you my reactions and results. The purpose of this operation is to avoid pulmonary embolism. Obviously, thrombosis, if there were no complications by embolism, would not be a very serious condition. It would cause swelling of the leg and some disability for a period of time. We all have seen many cases that have not had proximal ligation that have gone on to recanalization and complete recovery of the patient.

In my own series of 12 cases of thrombectomy from the iliac veins, eight have suffered from pulmonary emboli, and four have no outward evidence of embolism. Where thrombectomy has been performed, the use of an anticoagulant postoperative seems necessary. With proximal ligation, where one is above the clot, one does not fear particularly the recurrence of the disease except in patients who suffer from the migratory type of phlebotrombosis. I have had a much larger series where this procedure has been carried out without mortality, but am not reporting on them at this time. Where a thrombus has been removed above Poupart's ligament by suction or traction from below, it is obvious that a ligature is not applied proximal to the site where the clot was located. Therefore, it is advisable to use anticoagulants to prevent further thrombosis.

DIAGNOSIS

When a patient postoperatively is running a slightly irregular temperature, it is wise to pay attention to the foot, calf, and thigh. Homans has described the sign, which is now given his name, if the foot is flexed dorsally it compresses the gastrocnemius muscle, and pain is experienced in the calf. I have also found that if one semiflexes both knees, with the feet resting on the bed, the calf of the affected side gives one the feeling of a deep edema, and, as the gastrocnemius muscle is compressed against the posterior surface of the tibia, pain is elicited. Compression of the popliteal space may also present a tender area, or, if one passes the index finger horizontally across the thigh, pain is elicited over the course of either the long saphenous or Hunter's canal. On coming to Poupart's ligament the femoral artery does not give as clear a pulsation as on the noninvolved side, and beneath the artery may be felt a lead pencil-like cord, which is the thrombus in the femoral vein.

While venography has been advocated by Fine, and others, it is frequently difficult to determine whether the defect noted on the roentgenogram is due to venospasm or occlusion of the vein. Almost always, one can tell by physical examination, in the acute emergencies, more than one can tell from venography.

INDICATIONS FOR OPERATION

1 *Pulmonary Embolus with Evidence of Phlebothrombosis of the Veins of the Leg* If proximal ligation is possible there is no question but that this is the operation of choice and the treatment of choice, because it allows immediate mobilization of the patient without fear of the extension of the disease. If the thrombus extends above the iliac ligament, I believe that extraction of the clot, either by manual extraction or suction, followed by bisection and removal of a section of the femoral vein is the procedure of choice.

2 *Phlebothrombosis without any Evidence of Embolism* There are three methods of therapy that may be carried out when the diagnosis of phlebothrombosis of the deep femoral vein which extends upward into the iliac vein has been made. They are: First, incision of the vein and removal of the clot—phlebectomy. Second, the use of anticoagulants without surgical procedure. Murray, in Gallie's clinic in Toronto, has listed 18 successful cases of pulmonary embolism that have been treated by heparin without further evidence of pulmonary embolism. Others have not had as successful an experience. There have been a number of cases reported where death from embolism has occurred after heparinization has been discontinued. I had a case of my own that died from pulmonary embolism two days after heparin was discontinued. Third, novocaine block of the first to fourth lumbar ganglia. Leiche advocated this procedure primarily, and in this country it has been strongly advocated by Alton Ochsner. I quote from Ochsner's article to give you, better than I could brief it, the mechanism of this procedure:

"In previous publications we have discussed in detail the mechanism by which venospasm and thrombophlebitis can produce clinical manifestations. Edema may be due to factors that result from venospasm and increase the amount of perivascular fluid, increased filtration pressure, anoxia of the capillary endothelium, and diminution in the flow of lymph. The increase in venous pressure in thrombophlebitis has been repeatedly demonstrated. This obviously increases the filtration pressure, which favors transudation of fluid from the vascular into the perivascular spaces. Because of the associated arteriolar spasm and evidence of diminished vascularity, there probably occurs an anoxia of the capillary endothelium that increases its permeability, permitting an excessive exudation of fluid into the perivascular spaces and thus resulting in the production of edema. Once the fluid gets out of the vascular channels in such a case it has difficulty in getting back because of the increase in the pressure on the venous side. Probably of greater significance in this condition is the fact that the pump, which is responsible for the movement of the lymph, is lost. Several investigators have demonstrated that the movement of lymph is dependent on arteriolar pulsations. In the presence of marked venospasm and increased venous pressure, arteriolar pulsations are reduced to a minimum, and the lymphatic pump is thereby lost.

"This decrease in lymph flow results in the stagnation of the lymph fluid and the

accumulation of proteins in the perivascular fields, thus setting up a vicious circle, in that the pressure of the perivascular fluid approaches that of the intravascular field, tending to prevent absorption of fluid from the perivascular spaces into vascular channels. Such a vicious circle is broken by novocaine block of the sympathetic ganglia, which causes an interruption of the vasoconstricting impulses and thus produces a reestablishment of the normal exchange of the intravascular and perivascular fluids. It has been demonstrated that blocking of the sympathetic nerves increases the flow of lymph. As a result of vasodilatation, the blood supply to the capillaries is increased, anoxia of the capillary endothelium is relieved, and excessive exudation of the vascular fluid into the perivascular spaces is prevented. By the return of the normal arteriolar pulsations, the pump, which is responsible for the movement of lymph, is reestablished, and the perivascular fluid is rapidly carried away. Because of this, the edema of the extremity in a patient with phlegmasia alba dolens disappears within a relatively short time after the production of sympathetic ganglion block.

"Similarly, the other manifestations associated with thrombophlebitis are relieved, probably by the increased vascularity. Pain, which is one of the most prominent manifestations of thrombophlebitis, is relieved dramatically. Prompt subsidence of fever may also be explained on the basis of a more rapid resolution of the inflammatory process by the increase of vascularity to the involved venous segment."

Of these three methods I prefer thrombectomy, although I am free to admit that a certain number of unnecessary operations will be performed. If the patient is seen early after the initiation of the disease, thrombectomy is a relatively safe procedure, and is apt to eliminate the danger of pulmonary embolism. However, when the patient is first seen eight to ten days after the onset of phlebothrombosis, and where no evidence of pulmonary embolus has been present, I believe that we are safe in following a conservative course. It has been my experience that embolism usually occurs early in the course of thrombosis—occasionally even before its presence may have been diagnosed—in the thigh or leg, and that it is not as apt to occur after the clot has been formally organized. In the small series of eight cases that I have seen of this type no pulmonary embolus has developed.

OPERATIVE TECHNIC

Anesthesia—In many cases there has been pulmonary embolism of sufficient severity to contraindicate against general anesthesia. In such cases local anesthesia seems to be the one of choice. There is danger, as is shown in Case 12 of this series, that the position necessary for spinal anesthesia, with flexion of the thigh on the abdomen, might cause dissociation of a thrombus. Cyclopropane, where the case is early and without embolism, or with only slight evidence of pulmonary involvement, is also easier on the operator and the patient. *Local Anesthesia* No matter how carefully one blocks the field with novocaine there is a time when the vein is being separated from the artery that pain is present and cannot well be eliminated. Lumbar block might help at this time. When one opens the femoral sheath below Poupart's, in the cases I have operated upon there is a sticky, gelatinous adhesion of the artery and vein, and it is with considerable difficulty that the vein is sufficiently separated from the artery to allow an aneurysm needle to be placed about it and a traction ligature applied.

It has been my habit to expose the vein about an inch below Poupart's so as not to ligate below the profunda branch of the vein. After a traction ligature above and below has been placed, a longitudinal incision is made into the vein. The nearby blood clot is removed by forceps. Then a glass tube attached to a suction machine is inserted into the vein and passed upwards beneath Poupart's ligament until the thrombus has been removed and free bleeding occurs. If the tube is not long enough to permit free bleeding, a rubber catheter is attached and this is passed upward until one is certain that it has gone beyond the bifurcation of the vena cava. It is difficult, in the lower portion, to get enough suction to excise the clot through the smaller lumen of a catheter. A glass tube in this lower portion is much more efficient. I am convinced that the suction must be applied until free bleeding occurs. After the clot has been removed, the vein is doubly ligated on each end of the incision. The intermediary portion is removed. It is advisable at this time to look for the long saphenous, as it may also contain a clot, and, if so, it should be tied at its junction with the femoral vein. Usually I have ligated and cut both the long saphenous and femoral veins. If the femoral vein at the initial exposure is found in spasm, with only a small clot in its lumen, the long saphenous should be looked for. In two of my patients the clot extended up the long saphenous and thence into the femoral vein and upward into the iliac. The femoral vein itself was in spasm, with only a small clot within its lumen.

The use of anticoagulants is necessary in order to prevent the reformation of a thrombus above the ligated vein.

In this series of 12 cases, continuous intravenous heparin has been used in 5, dicoumarol in 2, and subcutaneous heparin, as described by Loewe, in 5.

In reviewing the following cases I have mentioned only those in whom thrombectomy of the iliac vein has been performed. Of the 12 cases, eight have had antecedent emboli, and four had no evidence of embolism. In this series, three had simultaneous thrombectomy and ligation of both femoral veins. One patient had a thrombectomy immediately preceding operation, and another case a thrombectomy two weeks previous to a supracervical hysterectomy.

CASE REPORTS

Case 1—A musician, a woman of about 50, had received a bumper fracture of the tibia. She had been treated by another surgeon. After her return home she had 12 pulmonary emboli—two nearly fatal ones. She had been treated by heparin intravenously for one week before I saw her but had shot one small embolus during this time. Her left leg and thigh were markedly swollen. There was only moderate elevation of temperature. In bed at home, under light gas anesthesia, the femoral vein was first exposed. It was in spasm and contained only a very small clot. It was doubly ligated and cut below the entrance of the profunda branch. The long saphenous was then exposed. It contained a large thrombus, which on exposure was found to extend into the iliac vein. The saphenous vein was opened, as much of the clot extracted as could be done with forceps, then a glass suction tube was passed upward into the femoral vein. Clots were extracted until the tube was passed upward about six inches,

when free bleeding occurred. The vein was doubly ligated and cut. Heparin was continued for three days. Her temperature rapidly subsided. In five days her left thigh and calf were the same size as the normal leg. Her convalescence was uneventful, and she had no more emboli, nor has she any residual swelling of the leg.

Case 2—A woman of 45, who had been ill at home with acute cholecystitis ten days before I saw her. At operation, I found a gangrenous gallbladder, with a perforated abscess in the liver. Cholecystectomy, with drainage, was performed. On the third postoperative day it was noted she had a swollen left leg and thigh. The long saphenous was palpable as a tender cord about the size of a lead pencil. On the fourth postoperative day she was operated upon and, under cyclopropane anesthesia, the femoral and long saphenous veins were exposed. Both contained large thrombi. By suction, a propagating thrombus about five inches long was removed from the iliac vein above Poupart's ligament. Both veins were doubly ligated and cut. She was treated with dicoumarin until her prothrombin index was one-third of normal, when it was discontinued. Her convalescence was uneventful until ten days later when she developed an acute phlebitis in the calf of the leg operated upon, associated with a chill, elevation of temperature, leukocytosis, and swelling and tenderness of the calf. The attack subsided under elevation and sulfa therapy. She had a residual swelling in the calf upon leaving the hospital. At present there is still some swelling of the calf.

Case 3—A young woman who had had an amputation of her left thigh at Memorial Hospital, for sarcoma. I saw her with Dr Stanley-Brown. She developed swelling of both thighs and shot two pulmonary emboli—left, then right. Both femoral veins were exposed simultaneously, under local anesthesia. On my side (the amputated one) no clot was encountered, but there was evidence of phlebitis. On Dr Stanley-Brown's side a clot was encountered extending well up into the iliac vein. A similar procedure was carried out as in the other cases. Heparin was administered five days postoperatively. Her convalescence was uneventful, and the swelling rapidly subsided in both sides.

Case 4—A woman of 53, upon whom a supravaginal hysterectomy had been performed by another surgeon four weeks previously. For the previous two weeks before I saw her she had had pulmonary embolic seizures, confirmed roentgenologically, and by Dr James Miller and Dr Harold Hyman. There was fluid at the right base. The left calf and thigh were moderately swollen. She was operated upon. Under local anesthesia, the femoral vein was exposed. It was occluded with clot, but the long saphenous vein was not involved. The clot extended upward about seven inches in the iliac vein. The same operative procedure was carried out, but, in addition, she had a lumbar ganglion block with novocaine. She had a moderate infection of the fat at the operative site in the thigh. She was given heparin subcutaneously by Loewe's method. Her convalescence was uneventful, and she had no residual swelling.

Case 5—A 68-year-old female, with a large ovarian carcinoma, had evidence of a thrombus in her right femoral and saphenous veins. At the time of operation a thrombus was removed from her right iliac vein and then a bilateral oophorectomy for tumors the size of a football was performed. She died on her 15th postoperative day from renal failure. There was no residual swelling of the leg or signs of pulmonary condition. No autopsy was obtained.

Case 6—A suprapubic prostatectomy was performed upon a 60-year-old man at Beth David Hospital. Postoperatively, while in the hospital, he shot several pulmonary emboli, and swelling of the left thigh and calf was noted. Despite this fact he was allowed to go home. After his return home he had several other episodes of pulmonary emboli. He was seen at home by Dr Solomon, who recommended his return to the hospital for thrombectomy. I saw him later at home and made the same recommendation. He was readmitted to the hospital. He was cyanotic, dyspneic, and had fluid at the right base. A similar operative procedure was carried out. He was treated first with

heparin and later, at Doctor Solomon's suggestion, with dicoumarol. His convalescence was remarkably uneventful after his dyspnea subsided, about four days postoperative.

Case 7—This patient had a supracervical hysterectomy three weeks previously. During the past week she had had three definite small pulmonary emboli. The left femoral vein contained a thrombus extending well above the inguinal ligament. A long thrombus above Poupart's was removed by suction. She was treated by subcutaneous heparin. She had some residual pain in the leg, but no swelling, for six weeks postoperative.

Case 8—A woman seen with Doctor Stanley-Brown at the New York Hospital. The patient was 62 years of age. She had had a coronary embolism in 1939. In February of 1943 she had a second coronary attack with three pulmonary infarctions. On April 14, 1943, she complained of pain in the right popliteal vein. On the 16th of April, heparin was started. On the 19th, I was called to see her by Doctor Stanley-Brown, and we found there was evidence of phlebothrombosis in both femoral veins. The femoral veins were exposed under local anesthesia. On the left side the vein was in spasm, and contained only a string-like clot. It was opened and a small clot sucked out of the lumen, and the vein then ligated. On the right side a long clot, extending well up toward the bifurcation of the vena cava, was removed. Both veins were doubly ligated and cut. Heparin was administered two days postoperatively, and the patient had an uneventful recovery. She was seen a year and a half afterward, at which time no swelling was noted in either thigh or leg.

Case 9—This patient had a normal delivery of a child on April 19, 1944. On April 25th swelling was noted in the left leg and thigh, and she had an attack of pain in the chest on May 9th. The patient was kept in bed and treated with rest. On May 15th, pain and swelling appeared in the right leg and the patient had another attack of pain in the chest. Under local anesthesia, both veins were exposed, and a clot was sucked out of each long saphenous and each femoral vein. Heparinization was administered for five days postoperative. Convalescence after this was uneventful, save that she had considerable swelling of both thighs, which persisted for six weeks. In a late follow-up I have learned that she is playing tennis, and, therefore, it is obvious that the swelling must have become greatly reduced.

Case 10—A woman of 46 had been seen by a gynecologist, who recommended hysterectomy for an extremely tender uterine fibroma which was fixed in the lower portion of the pelvis. The uterus extended midway to the umbilicus. Ten days later, while awaiting operation, acute phlebothrombosis occurred in the left femoral vein. I was called to see the patient at this time. There was no evidence then of pulmonary embolism. It was felt, however, that this patient would need hysterectomy in the near future because of a degenerating fibroid, and that it would be advisable to be sure that the clot was removed from the iliac vein. The clot was sucked out from the left iliac vein, and she was treated postoperatively by subcutaneous injections of heparin. Two weeks later, while still under heparinization, a supracervical hysterectomy was performed. The iliac vein was palpated and there was no evidence of any clot in its lumen. There were, however, some old thrombi in the veins of the broad ligament. This patient's convalescence was uneventful. She left the hospital two weeks after the hysterectomy.

COMMENT This patient was one of the few cases I have known where inspection occurred within two weeks of a thrombectomy. No evidence could be seen by the operating surgeon of occlusion of the vein.

Case 11—This patient had a cesarian section performed for a premature separation of the placenta in a seven-month pregnancy. A live baby resulted, and the postoperative convalescence of the mother was unusually smooth. There was no postoperative elevation of temperature, there was no complaint of abdominal or thigh pain.

The patient left the hospital on the 12th postoperative day. Three days later she complained of an acute attack of pain in the chest. She was readmitted to the hospital. Her temperature rose to 103° F. Three days after admission roentgenograms of the left chest showed irregular consolidation. Her physician had carefully gone over both legs and thighs, there was no difference in their circumference. There was no tenderness. Ten days after her admission into the hospital she had a sudden swelling and pain in the left thigh. I was called to see her on the next day. Under local anesthesia, the left femoral vein was exposed. A clot was removed. I did not feel, however, that I had reached the upper end of the clot because free bleeding was not obtained. It was in a strange hospital, there was some difficulty in getting the proper kind of tube, and I did not insert a catheter, as I should have, high up in the iliac vein, and I did not get as free bleeding as I wished. Her postoperative course was improved for about six days. Her temperature receded to almost normal, and she had no pain or swelling in the leg. However, eight days after the thrombectomy she had a sudden attack of pain in the right chest, with elevation of temperature. Roentgenograms showed a cloudy right lung, with not as great consolidation as on the other side. Up to this time there had been a question whether this was a virus pneumonia followed by a phlebothrombosis, or whether the initial infarct antedated the appearance of the phlebothrombosis by ten days. Eight days after the second attack of pain in the chest, phlebothrombosis developed in the right thigh. This time, under spinal anesthesia, a clot was removed from the left femoral vein, followed by free bleeding. The patient, however, went into collapse. She started to go into collapse during the administration of a low spinal, and her collapse continued after the removal of the clot. She was returned to her room in a serious condition. She lived three days thereafter.

Autopsy—"Lungs" The right lung is completely collapsed and attached to the chest wall by numerous strands of fibrin and purulent exudate. There are about 500 cc of a fibropurulent fluid in the right pleural cavity. The right lung weighed 400 Gm. The left lung is adherent at the apex to the chest wall by old fibrous adhesions. About 100 cc of thick purulent exudate are present in the left pleural cavity. The left lower lobe is completely collapsed. The left upper lobe is well aerated and pink in color. Examination of the branches of the pulmonary artery show a large thrombus in the lumen of the right vessels, with branches running to all of the lobes. This thrombus is yellow in color and adherent to the intimal layer of the vessel. On the left side there is a similar-appearing thrombus in the lumen of the branch of the left pulmonary artery leading to the left lower lobe. There is no thrombus found in the lumen of the main pulmonary artery. No mediastinal node enlargement is found.

"Uterus" The uterus is small and anteverted. The operative wound in the anterior wall of the myometrium is well closed by chromic catgut sutures, which are still present. Adherent to the anterior surface of endometrium is some granular pink tissue which grossly resembles placental tissue. The tubes and ovaries are essentially normal. The veins in the broad ligament of the right side are natural. On the left side the vessels at the base of the broad ligament contain distinct well-organized thrombic tissue. The vena cava and both iliac veins are opened. The right vein contains some postmortem clot which is lying free in the lumen of the vessel. On the left side, however, the blood clot in the iliac vein is well organized, yellowish-pink in color and adherent to the vessel wall. The thrombus runs up into the vena cava for a distance of 3 cm. At the upper end of this thrombus the blood clot is distinctly postmortem in nature. The branch of the hypogastric vein leading from the left iliac vessel is also thrombosed as are those of the veins in the pelvis on the left side. In the region of the left femoral vein the thrombus in the lumen of the vessels appears relatively fresh but distinctly postmortem."

COMMENT My impression of this case is that if I had been successful in removing the clot on the left side there probably would not have been an

extension of the process to the right side nor would there have been the later casting off of emboli. The unusual picture in this case was the time element, the development of the signs of the thigh ten days after the original infarct in each case. This was obviously a case which showered emboli from the pelvic veins, although on examination of the uterus there was no evidence of broad ligament involvement.

Case 12—A male, age 55, was operated upon for an inguinal hernia six years ago. His convalescence was complicated by a thrombophlebitis of the left thigh and leg. I am unable to determine whether this was a deep or superficial phlebitis. Following his convalescence he was well until six weeks ago, when he had an attack of phlebothrombosis of the superficial veins below the knee. After two weeks rest in bed he was allowed up. After being up and about for a week the process extended to the long saphenous vein. He was put to bed again for three weeks, with elevation and local heat. The phlebothrombosis gradually extended to the saphenous triangle. The day before I saw him he had a sudden severe attack of pain in his right chest, accompanied by shortness of breath but no bloody sputum. He was transferred to a hospital and operated upon. The long saphenous vein contained a clot which extended into the iliac vein. The femoral vein was exposed distally. It did not contain any thrombus. The thrombus was sucked out of the iliac vein and the saphenous was ligated and a portion excised. He was given heparin in Pitkin's solution, intramuscularly. His convalescence was uneventful.

COMMENT In the early stage it would have been so easy and safe to perform, under local anesthesia, a proximal ligation on this patient. He would have been saved weeks in bed, as he could have been mobilized immediately postoperative.

SUMMARY OF CASES

Twelve cases with 16 thrombectomies, including three simultaneous thrombectomies of both iliac veins, are reviewed. Case 11, with first a thrombectomy on the left side, and then, ten days later, a thrombectomy on the right, is reported as two operations because of the intervening time element. Two thrombectomies preceded operation, one immediately preoperative (the case of the carcinoma of the ovary), and the second two weeks before hysterectomy.

There were two deaths in this series, one not due to the disease, the patient dying two weeks postoperative of renal insufficiency. The second death was definitely due to the disease.

Only one patient had a later embolism.

Anticoagulants were used in all of the cases.

I should like to describe the method of using heparin subcutaneously, by injections at 2- to 3-day intervals, as developed by Leo Loewe, in New York. I quote from Loewe as follows:

"To accomplish a slower and more equitable absorption of heparin, the Pitkin menstruum was adopted as a vehicle. This menstruum was developed to regulate the rate of release of water soluble drugs injected intramuscularly or subcutaneously. The ingredients are gelatin, 15 to 30 per cent, dextrose, 5 to 12 per cent, acetic acid, 1 to 15 per cent, distilled water, q.s. to 100 per cent. The viscosity of the menstruum, which is predicated on the concentration of the gelatin and dextrose, determines the

rate of liberation of the drug, the greater the viscosity, the slower the liberation. In the preparations containing heparin the optimum percentages of gelatin and dextrose were 18 per cent and 8 per cent, respectively.

"Ampules containing varying proportions of heparin and Pitkin menstruum, with or without vasoconstrictor elements, were prepared. All ingredients apart from heparin were found to be inactive in control tests.

"The contents of the ampules were liquefied at 110° F, drawn up through a 25-inch, 19-gauge needle into a previously warmed, sterile 5 cc or 10 cc syringe and immediately injected subcutaneously, preferably in the anterior or lateral aspect of the thigh. Intragluteal injections were also done in a limited number of instances. Although this method of administration was abandoned because of too rapid absorption, further experience may eventually prove it to be just as effective as by the subcutaneous route. When two ampules were employed, the contents were thoroughly admixed in the syringe before injecting. The material congealed promptly following inoculation. The injections were administered with a minimal amount of discomfort to the patient. Some patients subsequently complained of pain, tenderness, and swelling at the site of inoculation, particularly when a large amount (3 to 4 cc) of the menstruum was used. This, however, did not prove to be a deterrent to further treatment, and symptoms promptly subsided upon cessation of therapy."

The results of Loewe's treatment are that it is possible now to heparinize a patient for ten days at a much less expense and with possibly three to four subcutaneous injections during this time.

My observations of Loewe's method show that it does lengthen the bleeding time, and that the patient has no ill effects from the treatment save for the pain in the injection area. This tenderness in the area where the heparin-Pitkin solution is injected becomes quite a problem as the patient may, about the time of the third injection, oppose the injection because of the pain involved. As the process is improved, however, I feel certain that this one difficulty will be remedied. To those who have had to give heparin constantly for from five to ten days, this method is a great improvement. The expense of the old method, and the amount of fluid given during each 24 hours, almost make continuous injection prohibitive in these days of diminished nursing care.

SUMMARY AND CONCLUSIONS

Twelve cases of thrombectomy of the iliac vein have been presented. Three of these thrombectomies were performed as bilateral excision of clot in each iliac vein. In this group there was one mortality due to an embolus. The postmortem examination and case history of this case are presented and discussed. It is the author's opinion that this procedure is safe, that it does not result in marked swelling of the leg, and is a life-saving measure in cases where emboli have already resulted.

THE ECONOMIC VALUE OF PERITONEOSCOPY

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PERITONEOSCOPY, or the direct inspection of the abdominal cavity with an endoscopic instrument, is a diagnostic procedure known to clinicians since 1901. The most important contributions toward its development are found in Table I.

At the Memorial Hospital our chief interest in this endoscopic field has been in the determination or recognition of the inoperability of various intra-abdominal neoplasms. One can frequently appreciate the inoperability of some cancers by this examination, but, on the contrary, the resectability can never be ascertained with any degree of certainty. If this fact were universally known, the limitations of the instrument would be accepted and no extravagant claims for its use would be made. The recognition of metastases in the liver or carcinomatous implants on parietal or pelvic peritoneum, for example, would discourage any surgical attempt at removal of a gastric cancer. On the other hand a cancer apparently confined to the stomach, as viewed through the peritoneoscope, may be definitely inoperable because of retroperitoneal involvement, infiltration around major blood vessels, etc. The diagnosis of cancer of the stomach and the majority of other intra-abdominal tumors has usually been established before peritoneoscopy is contemplated, so it is seldom employed for this purpose. The chief indication for its use, in our hands, is the attempted determination of inoperability, in borderline cases, when clinical evidence of such inoperability does not exist. With this point of view, one could not make the mistake of denying to any patient the opportunity for surgical relief or cure. If the criteria which determine inoperability are not fulfilled on peritoneoscopic study, a celiotomy immediately follows, and the tumor is then found to be resectable or inoperable. This discovery of inoperability should not be listed as a failure for peritoneoscopy, because it only confirms the well-recognized limitations and handicaps of the method.

This relatively safe minor procedure will often prevent useless exploratory celiotomies in patients who are poor surgical risks. The economic advantages to the patient, and to the hospital, will be discussed later in greater detail. Peritoneoscopy is generally indicated in the following conditions: Intra-abdominal tumors, particularly malignant tumors, cirrhosis of the liver, ascites of undetermined origin, tuberculous peritonitis, ectopic pregnancy, and lesions of the internal female genitals. The procedure is contraindicated in acute inflammatory conditions of the abdomen, advanced cardiac or pul-

monary diseases, and extensive peritoneal adhesions. The single death in this series occurred in a jaundiced patient, this fatality, from slow, hidden intra-peritoneal hemorrhage would not occur now, with the routine employment of prothrombin estimation and vitamin K therapy.

TECHNIC OF PERITONEOSCOPY

After preliminary sedation with morphine and scopolamine, the abdominal wall is prepared as for any celiotomy. In addition to sterile gowns and gloves, the operator, and his assistant, wear sterilized fiber masks and sterile

TABLE I
HISTORICAL DEVELOPMENT OF PERITONEOSCOPY

Name	Year	Contribution
1 Kelling	1910	"Kolioscope" — First demonstration made on a living dog. Used a cystoscope and was the first to inflate the abdomen with air.
2 Jacobaeus	1910	"Laparoscopy" — Received recognition for the procedure. Was the first to apply pneumoperitoneum to roentgenologic diagnosis.
3 Bernheim	1911	The first American to attempt peritoneoscopy. Devised a proctoscope of one-half-inch bore which he inserted through a small incision in the epigastrium. Head mirror used for source of illumination. Used the term "organoscopy."
4 Nordentoeft	1912	Devised a "trochar endoscope." Was the first to describe the endoscopic appearance of the female organs with the patient in the Trendelenburg position.
5 Nadeau and Kampmeier	1925	Published a complete description of the technic of endoscopy of the abdomen.
6 Ruddock	1937	Devised superior instrument. Outlined standard procedure. Introduced the term "peritonoscopy."

spectacles. The operating room is completely darkened. A site for the introduction of the instrument is selected in the midline immediately below the umbilicus. The skin, subcutaneous tissues, fascia, muscle and peritoneal fat are infiltrated with one per cent novocaine. A vertical incision, not more than two centimeters in length, is made, and the tissues are retracted with narrow right-angle retractors until the posterior rectus sheath and peritoneum are exposed. A small blunt trochar is introduced into the peritoneal cavity and air is pumped in by means of an attached hand bulb. After a good-sized air space is secured (determined by abdominal tympany), a large trochar is inserted, the obturator removed, and the telescopic lens introduced. Examination of the peritoneal cavity including the visible organs and the serosal and parietal peritoneum is then undertaken. The pelvic cavity and its contents are best visualized by placement of the patient in the Trendelenburg position, whereas, the liver, gallbladder and stomach are best seen with the patient in the extreme opposite position, *i.e.*, with the superior half of the body elevated by 20 to 40 degrees (Fig. 1). Proper adjustment of shoulder braces and footboard facilitates this procedure. The peritoneoscope should be kept close to the parietal peritoneum and advanced always in a relatively horizontal direction in order to avoid injury to the viscera. The introduction of the Ruddock stomach tube with illuminated tip is of some help, as it aids the observer by transillumination of this organ. The peritoneum, fascia and skin are closed by the insertion of black silk sutures.

The lack of a modern Ruddock peritoneoscope does not constitute a bar to successful peritoneoscopy. The examination can be successfully accomplished with a child's esophagoscope or a cystoscope, as we occasionally did 10-15 years ago.

END-RESULTS OF PERITONEOSCOPY

Since January 1940, peritoneoscopy has been employed upon 80 patients at the Memorial Hospital. Of these, 26 had primary gastric cancers, 12 had



FIG. 1.—A Preliminary introduction of trocar into peritoneal cavity. Note sterile face mask and glasses.
B Examination of upper abdomen with the body of patient inclined, so as to elevate the upper half.
C Examination of the lower abdomen with the patient in the Trendelenburg position.

cirrhosis of the liver, seven had neoplasms of the gallbladder or liver, and six patients with mammary cancer had peritoneoscopic visualization of their livers. The diagnoses in the remaining 29 cases (36.25 per cent) are found in Table II.

Of the 26 patients with carcinoma of the stomach, who were subjected to peritoneoscopy, the purpose of peritoneoscopy was satisfactorily fulfilled in 53.8 per cent (14 patients). In seven patients, metastatic cancer was found to involve the liver, parietal peritoneum, or both, and in this group a major operation was avoided. In seven other patients, whose gastric cancers were

occurred in the group of 80 patients, the result of intraperitoneal hemorrhage in a patient with cirrhosis of the liver and a low prothrombin level. No obvious source of bleeding could be found on postmortem examination. This single operative death may be contrasted, for example, with that for exploratory celiotomy for cancer, which is generally in the neighborhood of eight per cent.

The brief period of hospitalization is of economic significance to the patients. At the present time, the total minimum cost (exclusive of professional fees) to a patient occupying an inexpensive private room for two weeks is \$140. Add to this the routine charges of \$55 for anesthesia and the use of the operating room when a major operation, such as an exploratory celiotomy is performed, and the total amounts to \$195 without additional expenditures, such as nursing care, medicines and laboratory charges. This is in contrast to the sum of \$58.50, or the total expense for two days' hospitalization, including the operating room cost, when peritoneoscopy is undertaken on patients of similar financial status. For ward or clinic patients, a comparable financial saving occurs—\$86 minus \$15, the cost of exploratory celiotomy, and \$24, the cost of peritoneoscopy.

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SPONTANEOUS INTRA-ABDOMINAL HEMORRHAGE

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HEMORRHAGE within the abdomen and into the peritoneal cavity is not in itself uncommon. However, when we exclude bleeding of a genital origin in females, bleeding due to rupture of abdominal aneurysms and bleeding due to direct trauma, we find that the spontaneous rupture of a splanchnic vessel is very rare. It is this condition which has been termed "abdominal apoplexy" by some, with which this paper deals. To the best of my knowledge, only 26 instances in 25 patients have been reported since 1911. It is the purpose of this paper to report three additional cases which have been observed at Cleveland City Hospital during the past year.

It has been said that there is nothing pathognomonic in either the symptoms or the signs of this entity to permit certain preoperative diagnosis. Such has been our experience. However, after analysis of the previously reported cases, Cushman and Kilgore have described the syndrome and believe that it can be diagnosed with a certain degree of certainty. They state that as long as the hemorrhage is confined within the leaves of the mesentery that the pain is typically that of a dull, sickening type. The initial pain is usually sudden in onset, and persistent or gradually subsiding rather than colicky in nature. We would add that it becomes colicky if actual obstruction is present. It is usually accompanied, sooner or later, by vomiting. Neither does vomiting nor evacuation of the bowel relieve the pain. In 11 of the cases previously reported, the pain subsided only to recur in a few hours to several days. This obviously depends upon the site, amount and recurrence of the actual hemorrhage. When tension around the hematoma is released, sudden excruciating pain is experienced, this is followed rapidly by collapse and signs of shock if hemorrhage of significant amount occurs. This phase may be initiated by vomiting, by the use of purgatives or by mild physical activity, any of which may, in turn, reestablish bleeding.

A certain amount of leukocytosis is usually seen, and when the blood actually enters the peritoneal cavity this becomes even greater. The red blood count and hemoglobin determinations may be helpful, but these depend greatly upon the amount of bleeding and the state of hydration of the patient.

A point of more than academic interest is that 56 per cent of the reported cases had signs of arteriosclerosis and/or hypertension. The average age of the group was approximately 56. When carefully questioned, some gave the history of some physical activity when the pain was first noted, *e g*, carrying a heavy load or bumping into someone. The celiac axis was involved in 8 of the cases, the superior mesenteric and its branches in 13, and in three cases the origin of the bleeding was not found or stated. Of this

group, 19 patients were operated upon. Ligation of the bleeding point was carried out in seven, and no point of hemorrhage was isolated in 12. Five of the operated group (26 per cent) died. Only one case was diagnosed correctly and proven by operation.⁶ Two cases reported by Cushman and Kilgore, one of which is the only recurrent case on record, were not operated upon, and recovered. Roughly, one-third of the patients began with pain but did not go on to collapse, one-third after an indefinite period went into shock, rupture of the hematoma occurred so early in the remaining third of the cases that collapse was almost the initial symptom.

The cases which we report consist of three colored males ages 55, 43 and 55, respectively.

Case 1—H. G., Negro, male, age 55, was admitted January 3, 1944, with a chief complaint of epigastric pain. This had come on suddenly about three hours before admission, while lifting a shovel full of ashes. It was sharp and very severe, there was a tendency for it to bore directly through to the back and though present continuously there were times when it became colicky and more severe. He had vomited twice before admission and once shortly thereafter. His last meal had been one hour before the onset of pain, and his last bowel movement had been on the preceding day. He had felt perfectly well until one day previously when slight anorexia was noted. His past history revealed that he had had a penile lesion at the age of 17 which had never been treated.

Physical Examination—The patient was well-nourished and well-developed. Temperature 37.7° C, pulse 114, respirations 20. Blood pressure 84/70. He was perspiring freely. General examination was essentially negative other than that relevant to the abdomen. The abdomen was markedly tender over a small area in the left epigastrium, with some tenderness in the left lower quadrant. Some spasm was also present in the left upper quadrant. Slight rebound tenderness was present throughout. No masses were felt and no borborygmi were heard. Liver dullness was present. On rectal examination, good tone was noted and there was no pelvic tenderness. Red blood cells 4,160,000, white blood cells 8,800. The urine contained one plus albumin, specific gravity 1.028. Roentgenograms of the abdomen were negative, and an upright film of the chest showed no free air under the diaphragm.

Continuous gastric suction was instituted. After giving him intravenous fluids, including plasma, his blood pressure rose to 124/72, pulse 130.

Operation—Exploratory celiotomy was performed under procaine intraspinal anesthesia. A large number of clots and considerable free blood were found in the peritoneal cavity. An hematoma, the size of a grapefruit, was found near the hepatic flexure in the transverse mesocolon, the inferior leaf of which had a laceration about four inches long in it near its base. As much of the hematoma as possible was evacuated, along with the remaining blood in the peritoneal cavity. No definite bleeding point was seen. The laceration was then closed with continuous interlocking suture of No. 00 chromic catgut. The abdomen was closed by through-and-through No. 8 Dehn sutures. Blood pressure at the end of the celiotomy had risen to 170/130.

Except for some vomiting on his 11th to 14th postoperative days, he made an uneventful recovery, and was discharged, January 28, 1944, after a negative G. I. series. His blood Kline was ++++ in both diagnostic and exclusion tests. His condition was good when recently seen in the out-patient department.

Case 2—G. M., Negro, male, age 43, was admitted, January 13, 1944, with a history of generalized, vague abdominal discomfort of 48 hours' duration. Shortly after its onset he began vomiting and had continued to do so, being unable to retain food or liquids of any kind. He had had no bowel movements for three days, though he had taken several

laxatives since the onset of his present illness. The pain was more severe in the upper abdomen and right paraumbilical region and had not shifted in any direction since its onset. The past history was noncontributory.

On admission, his temperature was 38.8°C , pulse 96, respirations 28, and blood pressure 150/120. The patient was well-developed and well-nourished. The skin was dry and warm. General examination was essentially negative other than that relevant to the abdomen. The abdomen was flat and no visible peristalsis was present. There was moderate tenderness in the right epigastrium and right paraumbilical region, the latter point being somewhat more tender. Rigidity of the right rectus muscle was present. No borborygmi were heard. Red blood cells 4,800,000, white blood cells 13,600. The urine had a specific gravity of 1.035, and had 8 to 10 hyaline and granular casts and an occasional white blood cell and red blood cell in each high power field.

Because it was felt that he probably had high intestinal obstruction, a small amount of thin barium was given the patient and watched under fluoroscopy. It was impossible to fill the distal portion of the stomach. A plain film of the abdomen and a chest film were negative. Constant gastric suction was started and intravenous fluids, including plasma, were given. An exploratory celiotomy through a right rectus incision was then performed, under procaine intraspinal anesthesia. A large mass, about 10 x 5 cm in diameter, was palpated within the "C" loop of the duodenum. Incision was made through the gastrocolic ligament and then through the peritoneum, behind which the hematoma was expressed as completely as possible. No bleeding point was found and the peritoneum and gastrocolic ligaments were closed. No free blood was present in the peritoneal cavity. The abdomen was then closed, using chromic catgut in layers. He has been seen in the out-patient department on two occasions, and has had no recurrence of symptoms. His blood pressure was 170/94 and 145/100 at these times. Blood calcium, bleeding time and clotting time have been normal.

Case 3—O. W., Negro, male, age 55, was admitted, April 10, 1943, with a chief complaint of heart trouble and abdominal pain. He had been treated elsewhere for about four months because of shortness of breath with marked dyspnea on exertion, orthopnea and ankle edema. He also had been told that he had high blood pressure. Three weeks before admission he became worse and had been confined to his bed, about three days previously he had first noted vague abdominal pain which was more pronounced in the epigastrium and right upper quadrant. There had been some associated vomiting, the nature of which was also rather vague. On the morning of admission he had had a "fainting spell" accompanied by profuse diaphoresis and weakness.

On admission, his temperature was 37.2°C , pulse 108, respirations 28, and blood pressure 188/148. He was a well-developed but rather poorly nourished colored male, who was lying rather listlessly in bed and who was rather dyspneic. There was no cyanosis noted. His skin was warm and moist. The pupils reacted to light and accommodation, and fundoscopic examination revealed moderate sclerosis of the vessels with areas of degeneration and recent hemorrhages visible. The thyroid was not palpable. There was slight venous distention of the cervical veins. The lungs were clear to percussion and auscultation except for transient rales at each base. The left border of cardiac dullness was at about the nipple line. The cardiac rhythm was regular and no murmurs were heard. The peripheral vessels were tortuous and sclerotic. The abdomen was diffusely tender but this was more pronounced in the right upper quadrant. Only voluntary spasm was present. Each costovertebral angle was also tender. The liver was palpable one fingersbreadth below the right costal arch. A left hydrocele was present. The reflexes were generally hypoactive. Marked tenderness was present above the prostate. Red blood cells 3,800,000, hemoglobin 11 Gm, white blood cells 30,000. The urine was loaded with white blood cells. The impression was hypertensive cardiovascular disease with arteriolar nephrosclerosis and pyelonephritis.

Following his evening meal on the day of admission he vomited and then immediately fainted, remaining unconscious for about two minutes. He perspired freely and was slightly euphoric. His pulse was very rapid, thready and irregular. Marked dyspnea was noted. He responded fairly well to 50 per cent glucose and aminophyllin but remained lethargic. A lumbar puncture was done, mechanics and pressure were normal and a cell count of 26 was noted. The blood urea nitrogen was 51.8, and creatinine was 4.8. Surgical consultation confirmed the impression of bilateral pyelonephritis and uremia. Genito-urinary and chest films were negative except for the evidence of cardiac enlargement.

After three days the abdominal signs had disappeared completely except for accurate point tenderness in the right upper quadrant. His white blood count was 9,400, and the urine had essentially cleared. Blood pressure remained at a somewhat higher level than that recorded on admission, the highest figure recorded being 245/142. Vital capacity was two liters.

Digitalization was started. The patient appeared to improve until 14 days after admission when abdominal cramping pains started. They became progressively more severe and were associated with nausea and vomiting. When seen in surgical consultation he had exquisite tenderness and spasm in the right upper quadrant with some spasm throughout the entire abdomen. Moderate rebound tenderness and distention were present. The impression at that time was an acute exacerbation of chronic cholecystitis. A plain film of the abdomen and a chest film failed to show any sign of perforated intra-abdominal hollow viscus, however, two shadows were seen which were interpreted as gallstones. Because of his hypertension, with moderate cardiac failure and uremia, he was considered a poor surgical risk. On the following three days his abdominal tenderness, spasm and distention were markedly improved, when suddenly, on his 18th hospital day, he became dyspneic, his pulse went up to 180, and blood pressure was 100/60. Other signs of shock were present. The abdomen was very distended and tenderness and spasm were now chiefly in the left upper quadrant. His pulse and blood pressure were unobtainable 30 minutes later, and he died one hour later, without any response to symptomatic therapy.

Autopsy was performed and the following diagnoses were made: (1) Organizing hematoma at head of pancreas, with rupture through mesocolon near hepatic flexure and hemorrhage into peritoneal cavity (3100 cc of fluid, with a specific gravity of 1.024), (2) chronic cholecystitis, with cholelithiasis, (3) slight chronic pancreatitis, (4) marked bilateral pyelonephritis, (5) generalized arteriosclerosis, and (6) left inguinal hernia with hydrocele, bilateral.

Beneath the 5-cm rent in the hepatic flexure was a hematoma, about 10 x 8 cm in diameter. It did not involve the kidneys, the adrenals or any of the gastro-intestinal tract except the mesocolon and the "C" loop of the duodenum. The medial portion of the mass was in direct contact with, but definitely did not communicate with, the head of the pancreas. Exploration of the celiac and superior mesenteric vessels revealed no evidence of rupture or thrombosis. The walls of the bowel were intact. On the right border of this mass another mass, measuring 5 x 3 x 2.5 cm, was found. Its wall was 4 mm thick and its contents gelatinous, this was interpreted as being an older hematoma.

DISCUSSION—In selecting these three cases to report, and in reviewing the literature, every effort has been made to include only those which were truly spontaneous in origin. For this reason, one of the previously reported cases was omitted because of the circumstances, a deep epigastric vein had ruptured during labor. In our minds this could not be called spontaneous in origin. Another condition which may be associated with marked intra-

abdominal hemorrhage is acute pancreatitis. Recently, a patient with this finding was operated upon at City Hospital but, because of the extensive necrosis in the pancreas, that case is not considered here. Although our third case was in the general region of the pancreas, it was the opinion of the pathologist that this hematoma did not communicate with that organ.

All three of these cases had arteriosclerosis, with associated hypertension that was quite definite, all were males. The average age incidence was approximately the same as for the previously reported cases, although the former group varied from the age of 27 to 80.

Each of our cases represents a different stage in this condition. The first was operated upon following rupture of the intramesenteric hematoma into the abdominal cavity, the second was operated upon before this perforation had occurred, but the hematoma was causing intestinal obstruction. The third case shows what course repeated intra-abdominal hemorrhage may pursue. In neither of our operated cases was an actual bleeding point found and ligated, but both recovered. An attempt was made to correlate the type and location of pain each had with the anatomic findings, but in most instances this has been unsatisfactory. For this reason we are hesitant about describing any "typical" syndrome.

SUMMARY

1 Three cases of spontaneous intra-abdominal hemorrhage have been reported, two of these cases were successfully operated upon, the third being diagnosed at autopsy.

2 An analysis of the 26 previously recorded cases has been discussed.

3 Even though this is a rare condition, we believe that it should be held in mind as an aid in diagnosis of obscure acute intra-abdominal pathology. It should be emphasized, however, that the symptoms and signs of abdominal apoplexy are dependent upon the site, the amount, and the rate of bleeding.

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COMPARATIVE STUDIES OF CANCEROUS VERSUS NONCANCEROUS BREASTS*

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II ^AROLE OF SO-CALLED CHRONIC CYSTIC MASTITIS IN MAMMARY CARCINOGENESIS INFLUENCE OF CERTAIN HORMONES ON HUMAN BREAST STRUCTURE

WE DO NOT EMPLOY the term "chronic cystic mastitis" in the diagnosis of lesions of the breast, since it conveys no indication of the presence or absence of many characteristic histopathologic changes, moreover, it implies a common etiology for a variety of lesions, most of which are anything but basically inflammatory processes. The deficiencies of the term have been recognized by many writers, some of whom have proposed new designations not always without merit. This multiplication of terminology has been, perhaps, partly responsible for furthering the usage of the expression "chronic cystic mastitis," since it affords a means of escape from a more complicated nomenclature. At the present time no universal agreement exists as to the precise lesions that should be included under the term "chronic cystic mastitis." That these lesions are of multiple histologic type will be conceded by most observers, but when it comes to selecting the true representatives there is disagreement. Some authors seem to exclude nothing, but beyond this very liberal point of view the requirements become somewhat more strict. Our impression is that most writers are liberal. The term "chronic cystic mastitis" is so ingrained in the minds of some pathologists that this diagnosis of a locally excised portion of breast almost amounts to a surgicopathologic reflex. Such haphazard terminology leads to neglect of the actual histologic features present, and an accurate diagnosis demands an enumeration of actual lesions, even though it may enforce the employment of a rather complicated terminology. Even if a certain group of lesions is eventually accepted as component parts of "chronic cystic mastitis," it seems reasonable to list which of these are present when diagnosis is made in a given case. It is not assured that all of these lesions are of equal importance, and unless mentioned categorically, the determination of which constitute the important ones will continue to be delayed. There is further need for speaking in specific terms, since etiologic factors are still in dispute, and every assistance which might contribute to this problem should be given. Clinical correlation would be facilitated by more definite designation of pathologic lesions.

Much of the confusion that exists in the literature on the subject under discussion stems from the following sources. Too little regard has been given structural features that depend directly upon age. Reports on relatively scanty material are all too frequent. Very little attention has been

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directed to periodic changes related to the menstrual cycle, and, hence, physiologic alterations have been interpreted as pathologic. Observations of hormonal influences on the mammary glands of lower animals have been too freely transposed to the human female breast. Many studies have been made by reviewing old material which was not prepared with any particular objective, this applies particularly to cancer-containing breasts where little if any stress was laid on the noncancerous portion of the breast. Serial sections have seldom been used to trace the origin and distribution of certain abnormal proliferations. Many conclusions have been made on a statistical basis alone with no effort to establish a supportive morphologic relationship based on histologic traceability. Gross observations on fixed material commonly lead to certain errors that are avoided in fresh dissections. There has been a tendency to draw conclusions as to genesis from observations of lesions far too advanced to permit interpretation of origin. Failure to recognize certain changes as postmortem or post-excisional, as the case may be, causes misinterpretation. This is absolutely unavoidable if large sections of tissue are fixed in bulk.

Any point of view that one chooses to take concerning the causal relation of so-called chronic cystic mastitis to mammary cancer can be abundantly supported from the literature. The coincidental occurrence of cancer and so-called chronic cystic mastitis is variously reported. The most extreme figure is 100 per cent, found by MacCarty and Mensing⁸ in a series of 967 mammary carcinomas. The explanation for this high figure is at once apparent by quoting the histologic criteria employed by them: "By chronic mastitis is meant the presence of one or more of the following conditions: Fibrosis, hyalinized fibrosis, lymphocytic infiltration, distortion, partial or complete destruction of the glandular groups, obliteration or dilatation of acinar lumina, atrophy, hypertrophy or hyperplasia of the parenchyma." A histologic net of this sort would, indeed, trap the wariest breast. A contrasting report was made by Bloodgood⁹ in 1921 (page 541 of the article): "It is important to record that the histologic pictures shown in Figures 33 through 85, and 90 and 91, have never been observed in the breast of a patient whose glands showed metastasis, or who had definite cancer." When one reviews Bloodgood's photomicrographs, which encompass nearly every type of lesion commonly present in surgical specimens of breast, cancerous or noncancerous, he wonders what sort of study could have enabled the comment, and he must conclude that in Bloodgood's cases of cancer, little or no attention was paid to noncancerous areas. Between the two extremes just mentioned, almost any percentage of coexistence can be found. Charteris¹⁰ reported evidence of "chronic cystic mastitis" in 85 per cent of 48 radical mastectomies for cancer. The coexistence recorded by Rodman¹¹ was 15.5 per cent. In a long monograph Semb¹² used the terms "fibro-adenomatosis simplex (microcystica)" and "fibro-adenomatosis cystica." In 140 cases of cancer he found "fibro-adenomatosis" in 80 per cent, 40 per cent being of the "simplex (microcystica)" type and 40 per cent being of the "cystica"

type (Note that Semb's "cystica" group includes papillary lesions) Semb defined his histologic criteria accurately, but it is noteworthy that on page 275 he acknowledges that his determinations were made without regard to menstrual changes. Logie¹³ used the term "cystic mastopathy" and described the morphologic complex of lesions that it included. In 118 cancerous breasts, 67 (56.7 per cent) had evidence of mastopathia cystica. Many other reports could be cited but the preceding should suffice to illustrate the statistical disagreement concerning the coexistence of cancer and so-called chronic cystic mastitis. It is to be noted that most writers base their diagnosis of "chronic cystic mastitis" on a term of their own selection, on the presence of at least one of a varying group of histologic findings. Others make no mention as to whether a single lesion or multiple ones are required.

Suppose the presence of one or more of the following *pot-pourri* of lesions is adopted as being diagnostic of so-called chronic cystic mastitis.

TABLE XXI

1 Cyst(s)	7 Periductal mastitis
2 Duct papillomatosis	8 Fat necrosis
3 Blunt duct adenosis	9 Hyperplasia of duct epithelium
4 Sclerosing adenosis	10 Fibro adenoma
5 Apocrine epithelium	11 Tendency to fibro-adenoma
6 Stasis and distention of ducts	(fibro adenomatoid mastopathy)

Then, the 300 cases of mammary carcinoma studied here show the accompaniment of so-called chronic cystic mastitis in 83 per cent, while the incidence in the 200 noncancerous cases is 90 per cent. Each of the above lesions has been rather closely defined in earlier pages of this paper and each has easily recognized histologic characters. We have avoided including doubtful findings such as "fibrosis," "hyalinized connective tissue," "cellular connective tissue," "lymphocytic infiltration," "desquamation," "atrophy," "epithelial hyperplasia," and other similar terms. It is easy to see that with complete laxity in selection of criteria and inclusion of changes due to age and the menstrual cycle, the incidence would reach or approach 100 per cent for both cancerous and noncancerous cases.

The change designated as "hyperplasia of duct epithelium" may not constitute in every instance a definite pathologic finding, for it is not always easy to be certain of what constitutes the uppermost levels of normal, or whether apparent epithelial hyperplasia is in reality a chance tangential section of a fold in a duct, as demonstrated by Ingleby¹⁴. In preceding sections evidence has been presented to show that fibro-adenoma and "tendency to fibro-adenoma" do not tend to occur together with other proliferative lesions. If these three members are eliminated from the tabulations and only the first eight are included, the following figures result. The incidence of so-called chronic cystic mastitis becomes 74 per cent for the cancer cases, and 76 per cent for the noncancer cases.

Earlier in this paper inference was made that the lesion complex of "stasis and distention of ducts," "periductal mastitis" and "fat necrosis" was not primarily related to a certain group of proliferative and cystic

lesions. It was stated that this nonproliferative triad might occur independently of the proliferative group, *i e*, in the absence of these lesions, or that it might occur in unison with this group. In the latter instance, however, the only morphologic relationship appeared to be in those cases where the periductal mastitis, *etc*, seemed either incidental or secondary to anatomic obstruction. The nonproliferative triad did not furnish an anatomic source of origin for the development of cysts, papillomas, blunt duct adenosis, apocrine epithelium or sclerosing adenosis. If, then, in addition to the three lesions already eliminated from the initial group of 11 lesions, we omit stasis and distention of ducts, periductal mastitis and fat necrosis, there is a residue of the first five lesions listed in Table XXI whose characters may be summarized as "cystic and proliferative" (We have not included a probably related lesion, "primary lobule alteration," but this omission causes no appreciable difference in either the absolute or comparative determinations).

If we use the presence of at least one of the cystic or proliferative lesions as a standard for the diagnosis of so-called chronic cystic mastitis, this condition is found in 59 per cent of the 300 cancerous breasts, and in 65 per cent of the 200 noncancerous breasts. If multiplicity of lesions is made a requirement, the figures fall rapidly. When two or more lesions are required, the coexistence is 35 per cent in the cancer series, and the frequency is 43 per cent in the noncancer series. If three lesions are required, the corresponding figures are 17 per cent and 25 per cent respectively. These determinations are for the two classes of cases taken as a whole, and since the cancerous breasts average 49.5 years in age and the noncancerous ones 39 years, it is necessary to compare the incidence of the group of cystic and proliferative lesions by decades. This is given in Table XXII.

TABLE XXII
FREQUENCY OF CYSTIC AND PROLIFERATIVE LESIONS BY DECADES

Decade	Cancer Cases		Noncancer Cases	
	If One Lesion is Required	If More than One Lesion is Required	If One Lesion is Required	If More than One Lesion is Required
30-40	58%	37%	60%	40%
40-50	63%	47%	82%	60%
50-60	50%	15%	57%	30%

The immediately preceding figures, in general, show somewhat similar trends in the occurrence of these cystic and proliferative lesions in various age-groups whether the breast is or is not cancerous. Throughout, there is slight to moderate numerical preponderance in favor of the noncancerous breasts. Perhaps there is a greater actual preponderance in the noncancerous breasts than revealed by this study. It must be emphasized again that the determinations made in the noncancerous series are based almost exclusively on local excisions, and hence the entire breast cannot be represented. At the same time, however, it seems reasonable that these local excisions represent the most altered portion of the organ.

Various interpretations can be made from Table XXII. If one wished to discount (on statistical grounds) the influence of these five lesions on

the genesis of mammary cancer, he could state that they are somewhat more common in noncancerous breasts than cancerous ones, and that in women 50-60 years of age multiplicity of these lesions is twice as common in breasts free from cancer. On the other hand, it could be argued that the cystic and proliferative lesions are most commonly encountered in the ages 40-50, and that this decade produces more mammary cancers than any other. Or, one could consider the two conditions independent, but with certain temporal relationships and divergences which depend on the natural history of the two disease processes.

The references to other writers and the tabulations shown here should sufficiently demonstrate that the concomitant occurrence of cancer and so-called chronic cystic mastitis will vary statistically according to selection of lesions.

We have previously enumerated five lesions that can be described collectively as "cystic and proliferative." Their tendency to coexist has been emphasized and recorded in preceding tables. Certain morphologic interrelationships have been traced in former sections, while lack of morphologic relation to other stated lesions has been shown.

We have been unable to detect local factors in the breast that can be interpreted as causal. This statement is based principally upon study and observation of lesions in their earliest phases of development. The absence of detectable local factors and the anatomic and age distribution of these lesions suggest that they may represent a metabolic disturbance, and with the established cyclic histologic changes referable to the follicular hormone and the corpus luteum hormone, it is reasonable to suspect that imbalance between these metabolic agents may be etiologic. This viewpoint has been taken by Goormatigh and Amerlinck¹⁵. Their conclusions were based on the study of changes produced in the mouse breast after injection of folliculin for varying periods of time. In the alterations produced it was their opinion that the major rôle was played by the corpus luteum hormone, the effects of which were prolonged by the administration of folliculin. While one must admit some resemblance in the changes reported to the disease in the human female breast, some features are lacking. No real proof of true cyst formation is offered, and to speak of a dilated duct as "cystic" may be misleading. Suffice it to say that Goormatigh and Amerlinck conceded the parallelism of the mouse and human lesions to be "*quasicomplet*." Lewis and Geschickter¹⁶ support the hormonal theory of etiology. They speak of two types of chronic cystic mastitis. In one of these, cysts predominate, and these they term "cystic disease." In the other type epithelial hyperplasia predominates, and this they term "adenosis." These writers refer cystic disease to the effects of theelin and adenosis to the effects of progestin. We are unable to dissociate our material so sharply into two such categories as have Lewis and Geschickter, since the cystic and the proliferative lesions have been shown repeatedly in our tabulated results to show a marked tendency to coexist. Lewis' and Geschickter's classi-

fication will fit some extreme anatomic forms of the disease under discussion, but it deals principally with accented features and does not fit the majority of cases. Lesions produced in rats by Geschickter and Byrnes¹⁷ after treatment with various estrogenic substances have some features in common with the human form of "chronic cystic mastitis." Burrows¹⁸ injected male mice with estrin and produced changes which he considered representative of chronic cystic mastitis. Careful survey of his text and examination of the photomicrographs show some resemblance to the human disease, but this seems forced, and interpretation must depend as much upon one's attitude as upon the lesions produced. As in Goormatigh and Amerlinck's work, no definite evidence of having produced clearly isolated cystic structures is given. The cystic and proliferative lesions produced in rats by Eisen¹⁹ with crystalline estrogen represent a rather satisfactory counterpart of those found in "chronic cystic mastitis" of the human female. Taylor and Waltman²⁰ failed to reproduce in mice treated with estrogen in oil a lesion-complex comparable to "chronic cystic mastitis" of humans. Greene²¹ has made interesting observations on a spontaneous familial disease of the rabbit breast in which the lesions closely simulate cystic and proliferative lesions of the human female. He regarded the observed changes as comparable to those found in animals after long continued administration of estrogenic substances.

All of the foregoing work briefly reviewed has a common defect, namely, that conclusions depend on the findings in rodent breasts. If one adopts the point of view that the lesions produced are equivalent to those in the human breast, is the hormonal basis proved for the human disease? Or, if one adopts the point of view that the lesions are not equivalent to those in humans, does it disprove a hormonal basis? It may well be that the physiologic gap between the two species is too wide for mutual transposition of morphologic observations. So far as we have been able to ascertain, there has not been any reasonably adequate histologic study of the human female breast under known conditions of hyperestrogenism. Accordingly, no one can point to any group of pathologic lesions in the breast and maintain with certainty that they are due to this influence as, for instance, one may do in glandular and cystic hyperplasia of the endometrium. Adequate histologic data on breast lesions occurring under excessive administration of the corpus luteum hormone in women are also lacking. Normal cyclic changes and the changes seen in early pregnancy can be confidently related to specific hormonal influences, but abnormal histologic patterns at the present time must logically remain in doubtful status pending further investigation.

The statistical frequency of the coexistence of so-called chronic cystic mastitis and mammary cancer has engaged more attention perhaps than is deserved. Those who find in their studies a high rate of coexistence uniformly place more importance upon this finding than those who report a much lower coexistence. In our opinion a better proof of causal relationship depends upon showing a direct anatomic association rather than a mere statistical one. In other words, it must be demonstrated anatomically

that the lesions of so-called chronic cystic mastitis furnish the actual focal starting point or points for at least a certain number of mammary cancers. Though the most direct approach, this is at the same time the most difficult to achieve. This difficulty lies in the fact that mammary cancer, like nearly every other form of cancer, almost always is a far advanced process when it is first observed either clinically or microscopically. One is reduced to a minute group of chance findings in local excisions for supposedly benign conditions, or these may be added to in small measure by microscopic study of the macroscopically noncancerous portions of breasts that contain cancer. By so doing an occasional breast yields sections that show convincing transition lesions or foci that fulfill the criteria for true noninfiltrating cancer. These foci should have no continuity with an infiltrating tumor. Such examples as this in our own material are too few for us to make any estimate of how frequently cancer of the breast may begin in the various lesions that are part of the lesion complex "chronic cystic mastitis." Though unable to give precise figures we can confidently say that we have seen cancer begin in duct papillomatosis, solitary and multiple, cyst, apocrine epithelium and blunt duct adenosis. This has been more fully commented on in other sections. Over a long period of years, a bulky material tediously studied may produce enough very early cancers to make possible a fuller analysis.

To date, the most practical and useful approach to the problem of "chronic cystic mastitis" and cancer has been the clinical follow-up method. Greenough and Simmons²² followed for from one to 17 years a group of 83 women who had local surgical excisions for cystic disease. In 48 per cent of these, carcinoma of the breast subsequently developed. One should bear in mind in this connection that in 1914 some histologic diagnoses of carcinoma were made on lesions that would not be regarded at the present time as cancer. In Johnson's²³ 101 cases of cystic disease, 61 were followed for one to 20 years and no carcinomas developed. Bloodgood,²⁴ in 1932, gave the follow-up record of a group of 350 cases of chronic cystic mastitis that had been operated upon prior to 1921.⁹ Not one of these cases had developed evidence of mammary carcinoma. It should be noted, however, that the whole breast had been removed in 61.5 per cent, leaving but a small group of suitable cases. Similar results were reported several years later by Lewis and Geschickter.²⁵ Of 271 cases of "adenosis" followed more than five years, two had died with breast cancer, and of 252 cases of "cystic disease" followed more than five years, one had died from breast cancer. It is not clear how many of these cases had operations, but apparently most of them had simple excisions. No statement is given concerning any patients who might have been living with breast cancer or upon whom a successful operation for breast cancer had been performed. Klingenstein²⁶ reported the subsequent development of carcinoma after local excision in two patients of 54 who were followed for two to 11 years. Campbell²⁷ reported his follow-up records of 290 cases. He grouped these into "simple cystic disease" and "adenocystic disease." Of 190 cases of simple cystic disease treated by local excision, 62

per cent were followed five or more years, and in only one did breast cancer develop. Of 43 cases of adenocystic disease, 52 per cent were followed five or more years, and in none did breast cancer develop. There were 57 cases treated by simple mastectomy. Of these 62 per cent were followed five or more years and one case developed cancer in the remaining breast.

One of the most recent and extensive follow-up studies is that of Warren,²⁸ notable in that much effort was made to place his conclusions on a sound statistical basis. He used the Massachusetts statistics for the death rate for mammary cancer among females, and estimated that the annual attack rate was twice the death rate. In addition, the expected annual incidence of mammary cancer in the general population was calculated for each decade. Warren pooled cases from two sources, Toronto and Boston. There were 602 cases from Toronto, 419 of which were followed five years or more. Of 900 Boston cases in which follow-up was attempted, this was successful in 604. In these the follow-up ranged from five to 21 years. In these 1206 cases, mammary cancer later was found in 42. According to Warren, the number of cancers expected to develop in a group of this size in the general population is 13.16. In the 1206 cases, 301 were designated by Warren as "chronic mastitis" and 743 as "chronic cystic mastitis." In these two combined groups 35 cancers developed. Twenty-five of these cancers were in the Boston material, as opposed to an expected number of 6.6. When calculations were made for age-group rates, the author concluded that "the breast cancer attack rate for women with chronic mastitis and related lesions in the age-group of 30-49 years is 11.7 times the rate for the Massachusetts female population, in the group over 50 years of age, 2.5 times as great, in the entire group, 4.5 times as great." It is stated by Warren that there is no way of knowing how many women in the general population who develop chronic mastitis come under observation, but he *assumes* (italics ours) that the proportion seeking medical attention is large. In other words, he implies a low incidence of chronic cystic mastitis in the population at large. In this connection the work of Keynes²⁹ deserves attention. This investigator removed one breast from 116 consecutive autopsies on female patients and made careful gross and microscopic examinations. Fifty-nine of the 116 breasts showed lesions of chronic mastitis. Keynes defined chronic mastitis as "manifested by dilatation of ducts and acini, accumulation in them of the products of epithelial activity, infiltration with lymphocytes, fibrosis, and epithelial changes." These designations are very general and make a high rate of occurrence almost unavoidable. It is recalled that MacCarty and Mensing, on the basis of similar criteria, reported an incidence of 100 per cent in a large series of cancer-containing breasts. Our own examination of 54 breasts from the population at large indicates that this source of material presents a much lower incidence and degree of so-called chronic cystic mastitis than the cancerous or noncancerous surgical breast.

The reasons for the varying reports on the frequency of mammary cancer

after chronic cystic mastitis are not clear. The character of the follow-up may be partly responsible. One undesirable feature is that most of these follow-up studies are incomplete, inasmuch, as only half, or a little more than half, of the total of all cases are successfully traced. The importance of the length of the follow-up period has been stressed by Warren as well as the age of the patient when she came under observation. A further omission from nearly all reports is a statement relative to whether or not the subsequent cancer developed in the same breast treated by local excision or the opposite one. Another common omission is in failing to indicate how long an interval elapsed between the local excision and the clinical recognition of cancer.

Statistical follow-up studies have so far not produced conclusive evidence that any specific lesion or lesions which are a part of so-called chronic cystic mastitis are particularly apt to be followed by cancer. Perhaps this would be possible if enough material could be followed, but this would require a follow-up group of several thousand cases, an endeavor of discouraging magnitude. Hence, available follow-up studies are, in essence, determinations of how frequently mammary cancer developed following local surgical excisions for benign, nonsuppurative lesions of assorted types. We, ourselves, have no such follow-up records to report, but we have some data that may be regarded as a follow-up in reverse. This has been done by checking over the series of 300 mammary cancers to determine how many of these cases had previous local excisions for nonsuppurative benign lesions. In so doing, 12 (4 per cent) such cases were found and are tabulated in Table XXIII. Extending our observations to a larger number of cases, it was ascertained from the records of 1200 cases of operable carcinoma of the breast that 29 (2.4 per cent) had previously had a local excision of breast for a noncancerous, nonsuppurative lesion. For control purposes the history of previous breast surgery in 1200 cases of cancer in other locations was investigated. These cases comprised an equivalent age-group and included cancer of the skin of the head and neck region, the uterine corpus and cervix. In these 1200 cases of nonmammary carcinoma only 13 (1.08 per cent) had histories of previous local surgical excisions of breast. Of further interest, is the fact that 29 of the 1200 cases of carcinoma of the breast had already, at time of admission, had the opposite breast removed for carcinoma. In the 1200 cases of nonmammary cancer, only eight had previously had a radical mastectomy for carcinoma. Since cases of cancer of the breast have had approximately two and one-half times the number of previous local breast operations than have had cases of cancer in other locations, there seems to be a positive relationship between previous breast abnormality and the later development of cancer in that organ. This, in some measure, implicates "chronic cystic mastitis," since the lesions of this complex are so numerous in the local excisions. In passing, it is pointed out that the figures just given emphasize the tendency of mammary cancer to be a bilateral disease. This has been attested to in the past by Kilgore,³⁰ and Davis³¹

TABLE XXIII

Age at Time of Radical Mastectomy for Cancer	Age at Time of Local Excision	Cases in which Cancer Developed on Same Side of Local Excision	Cases in which Cancer Developed in Opposite Breast
55	41	Yes	
55	52		Yes
49	47	Yes	
44	34		Yes
45	33	Yes	
47	43	Yes	
47	18	Yes*	Yes
49	49	Yes	
43	29	Yes	
61	44		Yes
65	39	Yes	
40	33	Yes*	Yes
—	—	—	—
Total		9	5

* Bilateral local excisions in patients who later developed at different dates cancer of each breast

Table XXIII shows clearly that follow-up studies of five-year and even ten-year periods fail to discover many of the cancers that develop after local excision, and, thus, Warren's²⁸ stress on the importance of length of follow-up is repeated. In Table XXIII a ten-year follow-up period would have failed to show the development of seven of the 12 cancers, giving a percentage of 17 for later cancer development as opposed to the true figure of 4 per cent. We get the impression that these latter figures represent possible maximums and minimums, and give some insight as to why various follow-up reports of later cancer development are apt to vary in about this range.

The 12 cases in Table XXIII are far too few to allow any conclusion as to whether or not any specific lesion present in the local excision was frequent enough to suggest that it was of definite precancerous nature, *i e*, in a statistical sense. One finding, however, is of particular interest. Of the 12 cancer cases that had previous local excisions, the cancer developed in the opposite breast in three instances, and in two other cases bilateral local excisions were performed. These facts must be borne in mind when one weighs prophylactic simple mastectomy as a therapeutic procedure in so-called chronic cystic mastitis. In these 12 cases where cancer developed some time after local surgical excisions, there were five instances in which it was anybody's guess as to which breast should have been removed "prophylactically." On this basis, if any prophylactic surgical procedures are employed, they must be bilateral simple mastectomies, or a large portion of the prophylaxis will be lost, since one cannot predict which breast will be the site of cancer at a later date. The present authors by no means favor either unilateral or bilateral prophylactic simple mastectomy as a standard form of treatment. Part of the reason for this point of view has just been discussed. Furthermore, if a program of "prophylactic" breast surgery were undertaken at the Memorial Hospital alone, it would impose the non-radical removal of slightly more than 1000 breasts annually. On the basis of published estimates already quoted, one year of this aggressive surgery would theoretically prevent from 5 to 20 cancers. Patients would scarcely

elect such a procedure, and were it known that it was contemplated, it is likely that many otherwise willing women would be frightened away from examining physicians, and allow their cancers to grow in private. It is our belief that women who have had a local excision for a nonsuppurative, nonmalignant breast lesion should be examined at least twice yearly for a prolonged period of years, since observations made in this study indicate that these individuals are more subject to mammary cancer than other groups. No one debates the desirability of clinical follow-up examinations of women who have had a radical mastectomy for mammary cancer, and certainly a leading reason for this is to observe the opposite breast, the chance of cure in recurrent or metastatic mammary carcinoma after radical mastectomy is so small as to minimize the practical importance of such a finding, but this is not so when a second primary cancer is found in the opposite breast. In the 300 mammary cancers studied here, 14, or 4.7 per cent, had already had one breast removed for cancer, and it is certain that others will develop cancer in the opposite breast. These determinations indicate that if one advises prophylactic mastectomies in "chronic cystic mastitis," he must, likewise, if he is logical, demand prophylactic removal of the opposite breast in any case having a radical mastectomy for cancer. From the reports of others the impression is gained that simple mastectomy for noncancerous breast lesions is performed in other clinics much more commonly than at Memorial Hospital, where this procedure is undertaken in less than 2 per cent of noncancerous cases. The rationale of simple mastectomy in "chronic cystic mastitis," so far as we can ascertain, has not been clearly demonstrated. The performance of this operation for "chronic cystic mastitis" should be discarded until specific lesions are proved beyond doubt to be followed by cancer in a sufficiently high percentage of cases to warrant the procedure. Since in our series of 300 radical amputations for breast cancer, 14 of the patients had already had the opposite breast removed for cancer, the following statement is suggested. The one most common "precancerous" lesion of the left breast is a cancer of the right breast and *vice versa*.

Present data are not sufficient to determine with exactness the importance of so-called chronic cystic mastitis in the over all development of carcinoma of the breast. Morphologic tracing of early phases of mammary cancer implicates the lesions of this complex in exceptional cases, and the soundest statistical studies point to some positive relationship. Until more fundamental knowledge of etiologic factors in both diseases is known, the extent of the relationship cannot be stated.

X—HISTOLOGIC FINDINGS IN BREASTS AFTER ADMINISTRATION OF ESTROGENIC SUBSTANCE

Exhaustive studies have been made of the influence of estrogens on the rodent breast. A much smaller number has dealt with effects in other species including lower primates. Some of these have been referred to in previous sections, but a full survey is not possible in this communication. In reviewing many past communications, however, one is impressed by the extreme

variability in response of the mammary gland. Many potentialities exist and are modified by such influences as species, strain, age, amount and duration of hormone administration, individual susceptibility and the type of estrogen employed. It is thought by many that the action of estrogens on the mammary gland centers primarily on the duct system and that progesterone acts on the lobules. Not controverting this general belief but illustrating the futility of set rules in mammary gland response are observations of Lewis and Turner,³² who found abundant lobule growth and alveolar secretion in a virgin female guinea-pig that received 0.25 mg. of diethylstilbestrol for 20 days. In a female ovariectomized monkey, Gardner and Van Wagenen³³ found extensive development of mammary lobules after 136,000 international units of hydroxyestrin benzoate, given over a space of 21.5 weeks in weekly fractions of 4000–8000 international units. These authors did not regard the change induced as comparable to a lactating breast, but inspection of the published photomicrograph reveals structure certainly consistent with late gestational hyperplasia. It is stated³³ that, in the rabbit, complete lobule development requires combined action of estrogen and progesterone. Specific reference to the foregoing is made here, since in our Case 10, that follows, we observed in the breast of a stilbestrol-treated postmenopausal woman widespread lobule formation, indistinguishable by us from the lobule pattern of lactating breast. The explanation of structural changes in breasts of the human female based on finding analogies in lower vertebrates must be treated with prudence, even though these analogies are gathering force.

The problem of whether or not estrogenic substances constitute a possible causative agent in the formation of mammary carcinoma in humans has been much talked of but little written upon. We have been able to discover three papers^{34, 35, 36} dealing with cases of breast cancer that were recognized during or shortly after estrogenic treatment. The very paucity of such recorded cases is rather indicative of a trivial rôle, since usage of estrogens has been widespread for a number of years. In the nine estrogen-treated cases that follow herein, five had carcinoma and in one of these patients the disease was bilateral. At the present time, we prefer not to enter into a critical discussion of the merits of these and the three cases already recorded. Not until more cases are available can a competent analysis be made.

One major reason for not attempting analysis of this problem is the lack of accurate basic knowledge of the structure of the human female breast following treatment with estrogenic hormones. Present descriptions are few. Haagensen and Auchincloss³⁷ examined the breast tissue in four cases after estrogen treatment. From three of these there were adequate amounts of tissue. One case showed only dilatation of ducts. In the other two there was "histologic evidence of marked stimulation of epithelium of the breast. The gland fields were large and numerous. There were areas in which small ducts multiplied to give the picture of adenosis. There were many dilated ducts. Some formed small cysts filled with amorphous debris. Others were partly, or entirely, filled with proliferating epithelium. The changes re-

sembled, in a general way, histologic changes observed in the mammary gland of mice after treatment with estrogens." In a case treated with theelin, Friedman, Finkle and Antopol³⁷ spoke of "moderate proliferation of duct buds." Hoffman³⁸ studied breast biopsies in two cases before and after administration of Progynon B. The histologic descriptions and photomicrographs in these cases alluded to the production of "characteristic alterations" in the posttherapy sections. Since the nature of "characteristic" breast alterations due to estrogenic influence is still a lingering problem with the present authors, we were unable to assimilate these conclusions. Geschickter⁶ makes brief mention of having studied breast biopsies from five women who had received from 25,000 to 100,000 international units of estrone for one to two months. He refers to "extension of the ducts, increase in the number of their lining cells and proliferation of periductal stroma." That author believed that these biopsies duplicated the appearance of an adolescent breast.

The cases reported below have some points of more than passing interest, but, in advance, it is stressed that we believe they offer little that carries beyond the range of speculation.

CASE REPORTS

Case 1—L. S., age 41. Patient had a surgical menopause in 1938. Beginning in February, 1941, on account of menopausal symptoms, she received injections of theelin, 10,000 international units at weekly intervals. This therapy continued for several months and then there was a rest interval of six months. Following this the injections were resumed at the same rate and in the same amount as formerly, and these injections were continued until February, 1943.

In June, 1942, she noticed pain and a small area of swelling in her left breast. These symptoms disappeared in a few months, but in January, 1943, she became aware of a painless lump in her left breast.

When examined, February 24, 1943, the right breast was described as normal. In the 3 o'clock axis of the left breast, 10 cm from the nipple, was a rather well-defined area of thickening about 2 cm in diameter. This was freely movable, not attached to skin and thought clinically to be a fibro-adenoma.

On February 25, 1943, local excision of the above mentioned area in the left breast was undertaken.

Gross Examination—Specimen measured 6 cm in greatest diameter, and, on section, was composed principally of fat in which there were broad fibrous bands of breast tissue which contained no localized tumor, cyst or papillary lesion.

Microscopic Examination—Duct system not remarkable. Lobules moderately numerous. In general, the acini are few in number and quite small. In other areas, however, they are somewhat more numerous, of larger dimension, and show graded transitional stages of apocrine metaplasia. Mitoses not present. Many acini are collapsed but others have patent lumina and contain nongranular material which stains bright pink to grayish-blue. Hyaline membranes not seen about acini. Duct papillomatosis, blunt duct adenosis, sclerosing adenosis not present.

COMMENT—None of the above findings may be considered unusual in a breast five years beyond the menopause, with the possible exception that more lobular integrity was present than in the average case this far beyond the menopause. Transition phases in apocrine metaplasia will bear mention.

Case 2—J C, age 47 This patient's menopause occurred in the summer of 1942. Substitution therapy was instituted in September, 1943, and over a period of two months she received 12 injections of estromone, each of 10,000 international units. After this she received two injections per month, each of 10,000 international units, until January, 1944. During this course of therapy she had no subjective symptoms related to her breasts. On December 25, 1943, she accidentally discovered a lump in her right breast.

On examination, January 3, 1944, the left breast showed no significant findings. In the upper outer quadrant of the right breast was a deeply lying, freely movable mass, measuring about $4 \times 2 \times 2$ cm. Clinically, it was thought to be a fibro-adenoma or a cyst. Local excision was undertaken on January 5, 1944.

Gross Examination—Specimen measured $8 \times 6.5 \times 3.5$ cm. Eccentrically located was a 3 cm egg-shaped, delicately encapsulated fibro-adenoma which was soft and slightly edematous. Cut-surface lacked an intracanalicular appearance, and there seemed to be relatively little epithelial component. Adjacent breast tissue appeared diffusely fibrous with slight fat content. Six small cysts were present, 2-8 mm in diameter. Lobules appeared rather indistinct and small.

Microscopic Examination—Sections of the mass itself showed it to be almost diffusely fibrous, with its bulk made up of partly hyalinized fibrosis and partly with more cellular connective tissue. Epithelial components were very few in number, made up of moderately dilated, inactive looking mammary ducts. The tumor scarcely represented a fibro-adenoma in the true sense of the word and might be more properly interpreted as fibro-adenomatoid mastopathy. In the surrounding breast tissue were moderate numbers of mammary lobules. None of these had a characteristic cyclic pattern. Many showed old lobular sclerosing adenosis. Others appeared as expected in a postmenopausal breast, varying stages of atrophy being present. One large lobule had frequent component parts and appeared in an early stage of apocrine transition. There were several areas of blunt duct adenosis which appeared in early phase and quite active, with considerable papillary hyperplasia of lining epithelium. In addition, there was slight papillomatosis in other ducts which did not appear to be newly formed.

COMMENT—Perhaps the occurrence of relatively early blunt duct adenosis, with papillary hyperplasia should be mentioned. Again, the occurrence of early transitional stage in apocrine metaplasia should be noted.

Case 3—V S, age 30. In early December, 1939, she noted a lump in her right breast. She went at once to her family physician who gave her injections of theelin, 2,500 international units, three times per week for several weeks. This caused no local change in her breast and the dosage was increased to 10,000 international units three times per week for several more weeks. Again, there was no change noted locally, but a lump appeared in the right axilla.

When examined, February 27, 1940, in the central portion of the breast was a firm, irregular mass $5 \times 5 \times 3$ cm, firmly attached to skin. The axilla contained a hard 2 cm mass.

Radical mastectomy was undertaken, February 28, 1940.

Gross Examination—In summary, there was a firm infiltrating mammary carcinoma $4 \times 3 \times 2.5$ cm, which had no unusual characters. Surrounding breast tissue contained little fat. The lobules seemed more abundant than usual, in some areas suggesting irregular overgrowth. No gross cystic or papillary lesions.

Microscopic Examination—Sections of the cancer showed a fully malignant, cellular infiltrating duct carcinoma, Grade III. No unusual or unexpected pathologic changes were noted which had not been seen on innumerable other occasions. Multiple axillary nodes were involved. Mammary lobules were numerous, of uniform pattern, and the only abnormalities present were those referable to pressure and distortion due to continuity with tumor. The breast tissue contained no noncancerous proliferative lesion.

COMMENT—No significant findings in the breast tissue

Case 4—C D, age 39 In 1934, a clinical diagnosis of chronic mastitis was made No specific treatment was given until September, 1939 At this time, her left breast became firm, enlarged and tender She was treated for several months with injections of theelin, 100,000 international units per month Her symptoms were alleviated, and her breasts became equal in size by March, 1940 At this time, the left breast contained transilluminatable lumps Hormone therapy was discontinued In July, 1940, her left breast became smaller than the right and quite firm Another course of theelin injections was given, 200,000 international units in four injections Last injection was given on August 21, 1940

When examined, September 12, 1940, a large, fixed mass occupied most of the left breast Tumor was attached to skin

Radical mastectomy was undertaken, September 17, 1940

Gross Examination—Most of the breast tissue was replaced by infiltrating tumor That which remained was largely fatty No gross lesions observed except the cancer Multiple axillary nodes involved

Microscopic Examination—No cytologic features of note were found in sections of the tumor In the remaining breast tissue there were few lobules, and these showed retrogressive atrophic changes The only noteworthy lesion in the breast tissue was one area of blunt duct adenosis, the growth-pattern of which indicated an earlier than usual phase

COMMENT—Note again the character of the blunt duct adenosis

Case 5—H H, age 55 In October, 1943, she noted a lump in her right breast Two months prior to this her breasts had been examined and no mass had been palpated The lump was painful for a time but this subsided

Patient's menopause occurred in early 1941 Substitution therapy was begun in January, 1941 Between that date and May, 1941, she received 10,000 international units of theelin every two weeks From June, 1941, until October, 1943, she took tablets of stilbestrol by mouth These totalled 175, each 0.5 mg From October, 1943, until late February, 1944, she took one of these tablets daily

Examination, February 28, 1944, revealed moderately large, shotty breasts In the right breast an indefinite mass, about 2 cm in diameter, was felt adjacent to the areolar border in the 11 o'clock axis There were no secondary skin changes and no deep fixation

On February 29, 1944, the above mass was surgically excised

Gross Examination—Specimen measured 6 x 4 x 3 cm, and was tough and fibrous On section, were a few scattered cysts, the largest not over 1 cm in diameter. No other visible abnormality

Microscopic Examination—Breast tissue fibrous except for very small amount of fat Small cysts had no residual lining Ducts and lobules, particularly the latter, were greatly reduced in number Some lobules showed atypical epithelial hyperplasia, and a few had the characteristic appearance of lobular carcinoma *in situ* A few foci of apocrine epithelium were seen

COMMENT—Presence of a rare lesion, lobular carcinoma *in situ*, is noteworthy but justified no conclusion Apocrine metaplasia again present If hormone produced any alteration in this breast the effects were extremely focal, since the organ as a whole was very atrophic Evidence of regenerating ducts and lobules was not found

Case 6—A S, age 48 In 1939, an hysterectomy was performed In October, 1941, stilbestrol therapy was commenced She received injections of 1 mg every other day, without interruption, for two years This therapy was terminated October 20, 1943 The patient thought that she first noticed a lump in her left breast in October, 1942 She was not certain of the exact time of onset, but believed that the lump alternately would disappear and reappear She had no subjective symptoms referable to her breasts In September, 1943, she noted puckering of the skin in the region where she had noted the lump

When examined, October 19, 1943, the skin in the upper outer quadrant was dimpled, and there was an underlying 4 cm tumor which was firm, irregular and partly fixed

Radical mastectomy was performed, October 29, 1943

Gross Examination—The breast contained a typical infiltrating scirrhous carcinoma, 2.5 cm in diameter The breast tissue was more fatty than fibrous and contained many small cysts, the largest about 3 mm in diameter There were no other gross lesions The mammary lobules were inconspicuous

Microscopic Examination—The tumor itself was characteristic infiltrating duct carcinoma There was extensive intramammary lymphatic invasion, and one axillary node contained metastatic tumor The mammary lobules were very few in number Those present showed changes secondary to the presence of the tumor and obstruction of ducts Here and there was slight piling-up of the duct epithelium, and in one area distinct but slight papillomatosis Multiple foci of apocrine metaplasia were present, and there were occasional scattered foci of blunt duct adenosis of slight degree and of intermediate phase

COMMENT—No microscopic findings of note

Case 7—A G, age 38 For one year this patient had noted "tingling and drawing sensations" in her left breast For a similar period she had been aware of a palpable lump in the lateral portion of the left breast A somewhat more recent development was premenstrual breast tenderness, more apparent on the left than right

When examined, February 13, 1941, there was a smooth, rounded nodule, about 3 cm in diameter, in the lower outer quadrant of the left breast

On April 21, 1941, Progynon B injections were commenced Two injections were given weekly, each 6000 rat units Six such injections were administered Just at the conclusion of this therapy it was thought that the lump in the left breast was somewhat smaller and softer Following the hormone therapy her menses were delayed for three weeks The apparent alteration in character of the lump in the breast was temporary, and it regained its former character, remaining essentially unchanged On October 9, 1941, an endometrial biopsy was done, which showed a normal premenstrual pattern On October 16, 1941, Progynon B injections were again started and were given in 6000 rat units quantities twice weekly until ten injections had been administered On November 17, 1941, another endometrial biopsy was taken, and this showed highly typical glandular and cystic endometrial hyperplasia

Local excision of the lump in the left breast was undertaken, November 19, 1941

Gross Examination—Excised specimen measured 5 x 5 x 2 cm It contained an encapsulated, intracanalicular fibro-adenoma, 2.5 cm in diameter This was freely movable in its bed Adjacent breast tissue was almost entirely fibrous in character, and the lobules were inconspicuous No gross lesions seen such as cysts or papillomas

Microscopic Examination—Sections of the fibro-adenoma were not impressive The canalicular epithelial channels contained very orderly inactive-looking lining epithelium They were surrounded by connective tissue which, immediately around the epithelial canals, was arranged in an edematous halo-like fashion, such as is commonly seen in gynecomastia The cellularity of the connective tissue varied from almost hyaline to moderately cellular In the breast tissue the lobules were rather numerous, and

they varied from small to moderate in size. Lobules not homogeneous in structure. An occasional lobule showed old sclerosing adenosis. A fair number of the terminal ducts showed distinct but not marked stratification hyperplasia of lining epithelium. Some of the mammary ducts were putting out end buds but not forming true lobules. There was one distinct area of blunt duct adenosis in a distinctly early proliferative phase. Now and then, a lobule was found with changes suggesting very early sclerosing adenosis. Some of the acinar lumina contained pinkish or grayish-pink secretory material, others contained acini with collapsed lumina. No lobules seen that were distinctly characteristic of a secretory phase of the menstrual cycle.

COMMENT—Although there was no uniform alteration in either the fibro-adenoma or adjacent breast tissue, mention is made of the appearance of the earlier phases of both blunt duct adenosis and sclerosing adenosis. This may be of some speculative interest, inasmuch, as estrogenic therapy had been begun only about six weeks before the breast material was obtained. Her previous estrogenic therapy had been completed about six months before, and was not as great in amount as the later cycle of hormone therapy.

Case 8—M. M., age 39. In 1933, when she was 29 years old, this patient had a pelvic operation, following which her menstrual periods became irregular and scanty. For an indefinite period of years she had noted swelling of her breasts and pain just before menstruation. In October, 1941, estrogenic therapy was begun, and she received 10,000 international units of theelin weekly, and continuously, until October, 1943. In October, 1943, her family physician noted a lump in her left breast. During the period of hormone therapy the patient had no new subjective breast symptoms. No statement as to whether her premenstrual tension was increased or decreased.

When examined, October 19, 1943, there was a cystic mass, about 4 cm in diameter, located in the upper outer quadrant of the left breast 3 cm from the nipple. This mass was not fixed and there were no skin changes.

Mass in the left breast was surgically excised, October 29, 1943.

Gross Examination—Specimen measured 6 x 5 x 4 cm. There was a 3-cm smooth thin-walled cyst, contents of which had been evacuated. Surrounding breast tissue was diffusely fibrous and contained occasional cysts which varied from 1–2 mm in diameter. No other gross lesion was seen. The mammary lobules appeared rather small and sparse.

Microscopic Examination—Lobules adjacent to the cyst wall showed expected secondary alterations. Lobules and ducts relatively few in number. Scattered areas of slight papillary hyperplasia in small and terminal ducts. Most definite abnormality present was blunt duct adenosis. Recent proliferative phases of this lesion as well as intermediate ones were seen. One minute focus of sclerosing adenosis was found, not in florid phase. A good many ducts had end-buds, which did not form lobules, and yet did not approach blunt duct adenosis.

Case 9—P. N., age 20. In November, 1940, this patient began to have intermittent pain in the upper outer quadrant of the right breast. For several months this seemed to occur just before and during her menses. For four months prior to November, 1941, however, the pain was more intense, more frequent, and not related to menstruation. She had no other breast symptoms.

When examined, December 1, 1941, close to the areola in the upper outer quadrant of the right breast was a slightly irregular area of firmness, measuring about 4 x 3 x 2 cm. This area of induration was fairly well-demarcated. Several centimeters medial to this region was a discrete area, 1 cm in diameter, which felt cystic.

The patient was examined periodically over a period of about 11 months, with essentially similar palpable findings. On November 9, 1942, she was given injections of testosterone propionate two times per week, in single 25 mg doses. A total of 16

injections were administered, the last on January 5, 1943. The patient's last menstrual period began on December 29, 1943, and was described as normal. Toward the end of the testosterone therapy the lump in the upper outer quadrant was thought to become softer but did not disappear.

Local excision was undertaken, January 13, 1943.

Gross Examination—The excised specimen measured $9 \times 7 \times 2$ cm. It was more or less homogeneous in appearance, with no definitely localized lesion. The breast tissue was diffusely fibrous, and on the cut-surfaces were small numbers of rather small, glistening, slightly moist lobules. No gross cystic or papillary lesion was seen.

Microscopic Examination—The chief feature of the microscopic examination was the difficulty in detecting a distinct abnormality. The frequency of the mammary lobules was decidedly reduced but not remarkable. The mammary ducts were correspondingly few. Nowhere in the sections was there any evidence of an unusual degree of atrophy, such as faded landmarks of lobules formerly present. If one predicted from the lobule structure the phase of the menstrual cycle at time of operation, it would be placed in an early secretory phase. Specifically present were mitoses in the acinar epithelium but by no means difficult to find. Nothing of note was seen in the breast stroma.

COMMENT—This case is briefly recorded so as to present essentially negative findings after specific hormone therapy. We have only one other case treated with testosterone in which sections of the breast are available. This case was that of a young woman who received quite large amounts of testosterone for a considerably longer period of time than the preceding case. The second case did have extremely atrophic breasts, but was a doubtful object for comparison, inasmuch, as the breast tissue was secured post-mortem in a patient with extreme cachexia from extraordinarily generalized osseous and other metastatic mammary cancer.

Case 10—B. R., age 42. In May, 1943, the patient noticed a lump in her left breast. This was accidentally discovered, and was asymptomatic. No other breast symptoms.

The patient was known to have bilateral polycystic kidneys, with hypertension, moderate renal insufficiency, and multiple episodes of hematuria.

Her menopause occurred in 1939. Stilbestrol therapy was begun, October 29, 1942. The daily dose ranged from 0.1–1 mg. Treatment was continuous and lasted through the time of the surgical procedures to be mentioned below. Between October 29, 1942, and October 14, 1943, patient received 131.2 mg of stilbestrol. During this time there was no uterine bleeding.

On examination, July 23, 1943, there was a 3×2 cm nodule at the 6 o'clock radius of the left breast. This was irregular and hard. Right breast was described as normal. No specific statement as to the consistency of the breast tissue in either breast.

On October 15, 1943, left radical mastectomy was undertaken.

Gross Examination—The breast contained a 2-cm infiltrating carcinoma, of not unusual type. The breast tissue, however, was most remarkably altered. Its composition throughout was more or less similar, but not entirely uniform, since there were two large, not well-demarcated portions about 6 cm and 4 cm, respectively, in greatest diameter. These areas bulged slightly on section, but were not encapsulated and merged rather imperceptibly with the remaining adjacent breast tissue. The exposed surfaces were extremely cellular, due to innumerable lobular units which varied from one millimeter to several millimeters in diameter. These lobular members were very closely aggregated in the two large areas noted above, but were also present elsewhere in the breast in smaller number. The predominantly epithelial nature of these small and larger lobulations was obvious, and their cut-surfaces, which were grayish-white to

grayish-pink, were slightly elevated. Occasional fine granular streaks were seen in these areas.

Microscopic Examination—The tumor was a cellular medullary infiltrating duct carcinoma, Grade II, composed of large cells growing in plexiform sheets. No unusual cytologic change was detected in the tumor. Sections were taken from all portions.

FIG 44

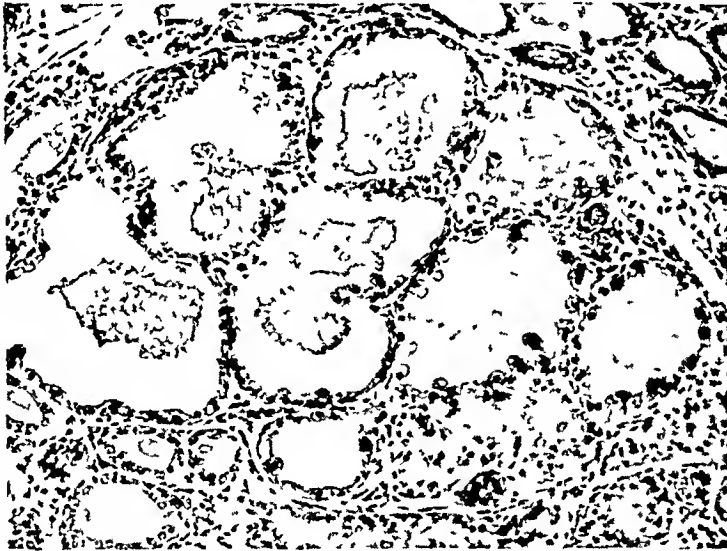
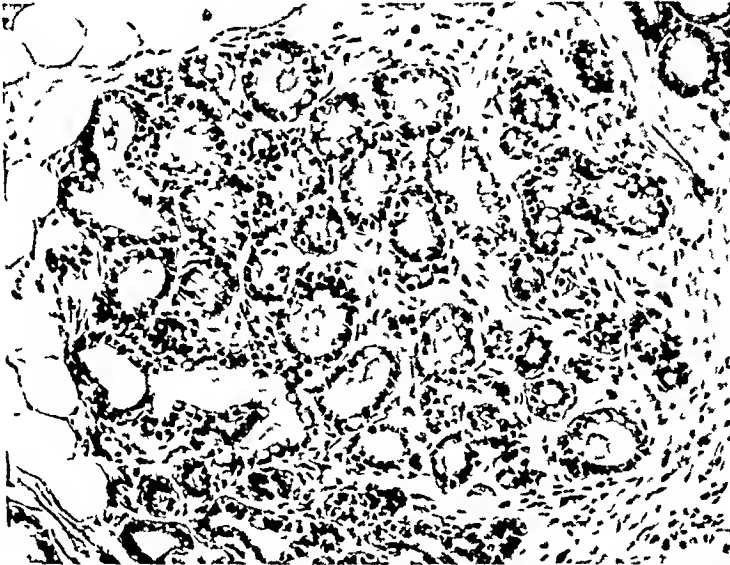


FIG 45

FIG 44—Lobule with structure indistinguishable from those of lactating breast. Patient postmenopausal. Received stilbestrol therapy (See Case 10 in text for details. Figures 44 through 47 are from the same breast.)

FIG 45—Similar to Figure 44, but showing exaggerated secretory structural pattern. At rare points cytoplasm becoming faint pink.

of the breast tissue, and these varied, one from the other, only in trifling degree. The composite structural pattern presented was unique and remarkable in degree, if not in kind—one not duplicated in thousands of mammary glands previously seen at this hospital. No segment of the breast was free from alteration. Here and there were scattered lobules without noteworthy configuration. These were exceptional. Almost everywhere would be met foci of sclerosing adenosis in florid phase. Merging with, and adjacent to, such lesions was much blunt duct adenosis in pronouncedly early

several times before sufficient material is available to point out trends in lesion types

In the present case there is one factor of possible consequence in the action of the stilbestrol that the patient received, namely, the presence of renal insufficiency due to polycystic kidneys. Perhaps with a deficient renal mechanism the excretion of this substance was retarded; and there was a resultant enhancement of action. The total amount of stilbestrol received over a period of one year in this case was not excessive.

In connection with this case we refer briefly to a recent publication of Engle, Krakower and Haagensen,³⁹ describing the results of intensive and sustained estrogenic administration to mature female monkeys. In their experiments the morphologic effects on the uterus, including glandular and cystic hyperplasia, far overshadowed any of the findings described in the breast. Another bit of evidence of threshold influence in mammary response is cited in the commonly unilateral nature of gynecomastia. Allen⁴⁰ found in male mice treated with estrogens that some of the mammary rudiments did not respond while others in the same animal did. The varied responses in mammary glands of different species are impressive. Since the breast tissue from the left radical mastectomy in Case 10 contained many areas structurally like late gestational or lactating breast, a recent experiment of Reece⁴¹ is of interest. By injecting diethylstilbestrol propionate he was able to induce full milk flow in sterile heifers.

Additional Note on Case 10 This patient's left radical mastectomy was undertaken on October 15, 1943. The stilbestrol therapy had been discontinued, October 7, 1943. On follow-up examination January 27, 1944, a one-centimeter mass was felt in the right breast. Aspiration biopsy was done and was reported as carcinoma. On account of the patient's generally poor physical condition, a modified mastectomy was performed, February 24, 1944.

Dissection of the operative specimen revealed a characteristic infiltrating carcinoma, 2.5 cm. in diameter. This had every gross feature of a new primary lesion. In the fibrous breast tissue there were multiple lobulated areas resembling sclerosing adenosis. No cysts or duct papillomata were seen.

Sections from the tumor disclosed a cellular growth-pattern, with large cells that had relatively abundant cytoplasm. At many areas in the tumor the cytoplasm was pale pink and sometimes finely granular, with more than casual resemblance to apocrine epithelium. The structure of this breast tissue showed many traits in common with that seen in sections of the left breast. Every lesion seen in the left breast was also observed in the right breast. The abnormalities were very widespread. Quantitative differences were apparent. One chief difference was considerable reduction in amount of tissue resembling lactating breast. Apocrine metaplasia was more in evidence. All transitional stages were represented. Papillomatosis in small ducts was more marked and had more atypical features. Sclerosing adenosis was more extensive and continued to be in florid phase. Actively proliferating blunt duct adenosis was present at multiple foci, and there were occasional intermediate phases of this change. Of interest was the fact that in the second breast mitotic activity, though not prominent, was more frequent in the abnormal lobular proliferations than was found in the preceding breast. In summary, comparison of these two breasts, sections from the second mastectomy revealed diminution of the lactation-like areas with moderate other proliferative phenomena.

COMMENT—Even though a second primary tumor developed in this case, it is still not easy to attribute its causation to hormone therapy. The tumor, 2.5 cm in diameter, was not a small one. It would appear safer to assume clinical oversight in the recognition of the tumor rather than to believe that no tumor was present when this patient was first examined in July, 1943, and at later visits. Just prior to the second mastectomy the tumor was described clinically as being one centimeter in diameter. The mere fact that it was 2.5 times this large forces one to suspect that the tumor was present long before detected. In view of preceding discussion, the resemblance of the cancer cells in many areas to apocrine epithelium is mentioned. Pink-staining quality was lacking in the cytoplasm of the cells of the initial tumor, but with this exception the cells in the two cases were comparable.

Whether, or not, the right breast tissue was structurally more like that of the left breast three months prior to the right mastectomy is, of course, impossible to say. To be sure, fundamentally, the same group of lesions was present in each breast with certain differences in degree as outlined above. Present observations are not sufficient to be sure that withdrawal of the hormone was followed by partial involution of the secretory looking areas. Nor is it possible to state that the more abundant apocrine epithelium found in the second breast represented a metaplastic by-product in such an involutional process. Other lesions including sclerosing adenosis, blunt duct adenosis and papillomatosis exhibited no regressive tendency in sections of the second mastectomy. No great importance attaches to this, however, for there is good reason to believe that they may maintain a fluid or active phase for long periods of time.

At most, this rather unique case furnishes guidance for future observations. A single case is not crucial, but a modest number of even less striking examples would reinforce a positive point of view, not only for the causation of certain noncancerous lesions by administration of estrogenic substances, but the modification of certain lesions following withdrawal.

In summary, the breast tissue from nine cases treated with estrogenic substances has been examined. The structural characters of these breasts were not sufficiently specific to constitute a distinct pathologic complex. Similarities as well as dissimilarities were present. Changes of kind and degree were found. One case was regarded as highly exceptional. Some suggestion of trends may be proposed such as the finding in several cases of earlier phases of blunt duct adenosis, sclerosing adenosis and apocrine metaplasia. The occurrence in one case of lobular carcinoma *in situ* calls for continued attention to this lesion. Over a long period of time enough material may accumulate to support or reject whatever point of view one now chooses. The pleomorphic character of various responses of the mammary gland may in the future be largely explained on a basis of individual susceptibility and reactivity.

CONCLUSIONS

1 Atrophy of the breast as judged by the number of lobules present depends upon the factor of age, and does not differ in cancerous *versus* noncancerous breasts

2 Macroscopic cysts are much commoner in noncancerous breasts, particularly in women between 40 and 50 years of age. During this period they are least common in cancer-containing breasts

3 No distinct difference in the frequency and extent of duct papillomatosis is found in cancerous and noncancerous breasts. Macroscopic papillomas are somewhat more common in noncancerous breasts. Cancer-containing breasts are about five times as apt to show papillomatosis which is cytologically atypical

4 Every transition from atypical papillomatosis to duct cancer can be traced microscopically, such phases being demonstrable on occasion in a single breast

5 Blunt duct adenosis appears to be a common precursor to cyst formation. In cancerous breasts between the fourth and fifth decades blunt duct adenosis is the most common, and cysts are comparatively few, indicating in this class of breasts, that blunt duct adenosis tends to retain its proliferative capacity

6 The origin of mammary cancer can be traced histologically to blunt duct adenosis in only a very few cases

7 Apocrine epithelium is common in both cancerous and noncancerous breasts, and of not pronouncedly different character. Rare cases of mammary cancer can be traced to this source

8 Sclerosing adenosis in cancerous as opposed to noncancerous breasts shows no outstanding differences. The early or "florid" phase is more common in younger women, but can be observed as late as the sixth decade

9 The triad of lesions including stasis of duct content, duct dilatation and periductal mastitis exhibits similar traits in both cancer and noncancer-containing breasts. No evidence was obtained that they furnish a starting point for development of mammary carcinoma

10 Two forms of periductal mastitis can be distinguished—primary and secondary. The latter is more common

11 Structural abnormalities of the mammary lobules are described. These can be separated into two groups referred to as primary and secondary lobular alteration

12 Intralobular hyperplasia of pathologic type can be shown in some cases to merge gradually with lobular mammary carcinoma *in situ*

13 Evidence is presented that the true component parts of "chronic cystic mastitis" should include (1) cysts, (2) duct papillomatosis, (3) blunt duct adenosis, (4) apocrine epithelium, and (5) sclerosing adenosis. Perhaps a sixth lesion, primary lobular alteration, may be included. Fibroadenoma is excluded

14 Estimations of the frequency of so-called chronic cystic mastitis

depend upon what and how many lesions are deemed essential in making that diagnosis

15 Statistical and morphologic studies indicate that chronic cystic mastitis does play a rôle in the development of human breast cancer. How large this is we cannot state. Our studies suggest that its part consists largely in those papillary hyperplasias which in some individuals, for reasons unknown, become cytologically atypical. In other words, some people cannot handle the hyperplasias which to others seem controllable and innocuous.

16 The pathologic findings in breasts from nine women treated with estrogenic substances are recorded. In one case remarkable structural features were present and these were fully discussed.

17 The failure of the breast tissue to respond uniformly to administration of hormone may depend upon individual differences in susceptibility. Thresholds of reactivity may vary through a broad range. Judged by the few cases available for study to date, wherein, with one notable exception treatment by estrogens has produced no noteworthy specific alteration in breast structure, one can at least say that no progressive series of changes beginning with a normal breast and ending with mammary cancer has been encountered. In the exceptional case, whereas, hormone alterations were, indeed, profound, there were reasons to doubt their significance in the production of the cancer.

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STUDIES IN SURGICAL CONVALESCENCE*

II. A PRELIMINARY STUDY OF THE NITROGEN LOSS IN EXUDATES IN SURGICAL CONDITIONS

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THIS REPORT, an outgrowth of studies on the nitrogen balance in surgical conditions, represents an attempt, quantitatively, to determine how much body proteins in the form of nitrogen is lost in the exudates of exudative surgical conditions. The values are random ones, and are reported out of their case-setting because, in many cases, they are of such magnitude as to be of importance to the practicing surgeon. It is apparent that unless large losses are replaced by special measures of alimentation, recovery from these conditions will be retarded or even jeopardized.

Thirteen cases, typifying four surgical conditions are included in this report. They are (1) Surface burns, (2) avulsion, (3) seepage from areas of extensive surgical dissection, both infected and uninfected, and (4) local infective conditions, such as lung and liver abscess.

METHODS

A number of difficulties attend the collection of material from an actively exuding surface. Surgical gauze dressings do not lend themselves to this purpose quantitatively because their retentive capacity is small, resulting in an overflow which seeps through into the bedding. Moreover, gauze is difficult to dissolve, sometimes taking as long as a month to six weeks to attain complete solution in sulfuric acid. Accordingly, in only three cases was gauze used. In ten, the following method of exudate collection was followed. Slabs of fine cellulose sponge (Du Pont) 0.25 x 10 x 5 inches were rendered nitrogen-free, by soaking them first in tap water for at least 12 hours and then rinsing them in distilled water three times. After drying at room temperature for about 24 hours, they were wrapped in cloth and sterilized in the autoclave. Before being applied to the exuding surface, they were moistened with physiologic saline solution. After application, the slab was covered with cellophane of medium thickness, extending beyond the edges of the sponge for about five inches, *i e*, far enough to prevent seepage.

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of the exudate beyond the edges of the cover. This sponge was usually left in contact with the exuding surface for from 24 to 48 hours. At the end of this period, it was transferred to dilute sulfuric acid for digestion. Both the cellophane covering and the skin beyond the exuding surface were wiped with pieces of moistened cellulose sponge, which were, likewise, placed in the sulfuric acid together with the sponge-dressings. It took about a week to bring the sponge into complete solution, after which an aliquot part was taken for nitrogen determination according to the method of Levy and Palmer¹

RESULTS

Table I summarizes all the 13 cases, with columns showing the nitrogen loss in terms of proteins and cubic centimeters of plasma.

Table II is a rearrangement of the cases of burns listed in Table I, in the order of the percentages of body surface involved. F W was listed twice in the table and J Mc three times, because their exudates were collected, one, twice, and the other, three times at different age-periods of the burns. There seems to be a rough parallelism between the percentage of body surface involved and the magnitude of nitrogen loss. However, other factors enter here to modify the picture, namely, how much of the wound is involved in second and how much in third degree burns, and how much tissue has been converted into an eschar, which would seal off exudation until it is sloughed off. Thus, while J Mc, whose burns were mostly second degree, showed a progressive decline in the magnitude of nitrogen loss as the burned area aged, F W showed a small loss of 1.58 Gm on the eighth day, when the burned area covered only 10 per cent, while on the fortieth day, when the burned area covered only 8 per cent, it was 4.07 Gm. J Mc had a burn which was not covered by an eschar, while F W's burn was. The figures for M W and A F were, respectively, 6.45 Gm and 9.17 Gm, representing 40 per cent of exuding surface on the ninety-fourth day and 50 per cent on the fourth day, respectively, were minimum figures since gauze was used for collection. These figures merely signified that at least this amount of nitrogen loss was sustained.

J Mc's figures suggested the possibility of an attempt on the part of the body to reduce nitrogen loss as the wound aged. The values of Hirschfeld, and his coworkers² seem to confirm this tendency. However, as mentioned before, this tendency would be modified by the presence of an eschar, and perhaps by other factors to be mentioned later.

Polar planimetry was performed on four of these cases in order to determine the nitrogen loss per unit area. The loss ranged from 1.25 mg on the sixth post-burn day, in J S, to 2.95 mg for the tenth day in F W, and 3.28 mg for the twelfth day in J W.

S S is an example of the second type. He suffered an extensive avulsion of the back, buttocks and perineum. The skin surface was infected and the exudate was of a seropurulent character. His loss of nitrogen was 6.37 Gm.

TABLe I
NITROGEN LOSS IN DIFFERENT EXUDATIVE SURGICAL CONDITIONS

Name and Sex	Diagnosis	Date of Injury or Operation	Date of Collection	Surface Involved Sq Cm	Total N			No Exuded in		Equiv in Plasma CC*	Collecting Material
					Exuded in 24 hrs	Gm	In 24 hrs	per Sq Cm In 24 hours	Equiv in Proteins Gm		
M W (M)	Burns 2nd and 3rd°	2/ 8/43	5/11/43	10	6 45+				10 31+	672+	Surg † gauze
A F (M)	Burns, 2nd and 3rd°	6/ 3/43	6/ 7/43	50	9 07+				58 80+	345+	
J Mc (F)	Burns, 2nd and 3rd°	7/ 1/43	7/ 7/43	30	5 15				32 19	537	
			7/18/43	21	3 56				22 25	373	
			7/22/43	15	2 98				18 62	310	
A B (F)	Burns 2nd and 3rd°	11/10/43	11/12/43	20	1 5				9 4	150	
J W (F)	Burns, 2nd and 3rd°	12/21/43	1/13/44	15	7 65		3 28		47 79	798	
F W (F)	Burns, 2nd and 3rd°	1/15/44	1/23/44	10	1 38		0 9		9 64	164	
			2/25/44	8	1 07		2 05		25 44	424	
J S (F)	Burns, 2nd and 3rd°	2/ 4/44	2/ 8/44	15	1 79		0 64		11 39	189	
S S (F)	Avulsion of perineum and back	7/ 7/43	10/23/43	15	6 37		2 1		39 81	664	
R W (F)	Radical mastectomy	10/25/43	10/26/44		4 20				26 65	445	
			10/30/44		1 2				7 50	125	
A G (F)	Abdomino-perineal resection (cancer of rectum)	8/13/43	8/14/43		6 22				38 87	644	
O Mc (F)	Abdomino perineal resection (cancer of rectum—Infected)	8/ 9/43	8/16/43		2 07				12 97	216	
			8/18/43		6 97				42 48	707	
F C (M)	Lung abscess—Pyothorax	4/17/43	8/21/43		3 47				21 68	723	
H L (M)	Liver abscess (5 cm diam)	12/26/43	4/24/43		9 57+				59 8+	393+	Surg gauze
			12/28/43		1 38				12 63	210	Cell † sponge

* The assumption is made that the protein content of plasma is 6 gm %

† Surg =Surgical ‡ Cell =Cellulose

TABLE II

CASES OF BURNS REARRANGED ACCORDING TO PERCENTAGE OF BODY SURFACE INVOLVED

Name	Body Surface Burned	Age of Burns (Days)	Nitrogen Loss (Gm)
1 F W	8%	40	4 07
2 F W	10%	8	1 58
3 J Mc	15%	21	2 98
4 J W	15%	23	7 65
5 J S	15%	4	1 79
6 A B	20%	2	1 5
7 J Mc	21%	15	3 56
8 J Mc	30%	6	5 15
9 M W	40%	94	6 45
10 A F	50%	4	9 07

on the 108th day after injury, representing 21 mg of nitrogen loss per sq cm of raw surface, equivalent to 39.2 Gm of protein, or 654 cc of plasma. This patient was kept in excellent nutritional condition and gained weight in spite of the nitrogen loss, which must have been of considerably larger magnitude during the earlier course of his convalescence.

The third type consisted of two conditions in which, as a result of extensive dissection, areas of raw exuding surface had been exposed. In R. W., a radical mastectomy was performed, the exudation of nitrogen in the blood-tinged fluid was 4.26 Gm during the first 24 hours, dwindling down to 1.2 Gm after four days, a decrease of approximately one-third of the original value. A. G. was a case of abdomino-perineal resection for carcinoma of the rectum. The exudate in the first 24 hours contained 6.22 Gm of nitrogen, dwindling down to 2.07 Gm on the third day, which was less than half of its original value. The values in these two cases suggest a tendency in clean operative wounds to rapidly seal off exuding points.

On the other hand, infected operative surfaces cannot be expected to reduce exudation as promptly. This seems to be true of O. Mc., who was also a case of abdomino-perineal resection, frankly infected, the infected area having been drained secondarily, nine days postoperatively. Here the nitrogen exudation was 6.97 Gm the day after drainage was instituted, decreasing to 3.47 Gm in five days. H. L. was a case of liver abscess, 48 hours after drainage was instituted, and F. C. a case of lung abscess with secondary pyothorax. Since gauze was used for the collection in this last case, this loss of 9.57 Gm of nitrogen is also a minimal figure.

DISCUSSION—The protein loss in the exudates in burns and other surgical conditions has not attracted serious clinical attention until recently. Lucido,³ in his metabolic study of one case of burn, to our knowledge the first one to be attempted, recognized the incompleteness of the study when the nitrogen lost in the exudate could not be determined. The report of Taylor's group⁴ on the difficulty of maintaining nutrition in the cases of burns involving over 10 per cent of body surface suggests the importance of undertaking such a study. Hirschfeld and his group have made a promising beginning, introducing a practical method of collection. Unfortunately, only one of their cases had extensive burns (35 per cent), the others involving only from 3 to 5 per cent of body surface. The report of Co Tui's group⁵ on the

comparative ease with which cases of extensive burns may be kept in good nutrition and at a fairly normal plasma level by hyperalimentation with amino-acid mixtures (Amigen) suggests a way of adequately meeting the need for the large amount of protein replacement sometimes impossible to effect by feeding natural food. These last authors also used polar planimetry in order to determine quantitatively the loss per unit area.

If the variability of the protein content reported in the literature on blister fluid is an indication, the amount of protein lost in the exudate would be expected to vary within a fairly wide range. Thus, Morner,⁶ in 1895, reported the protein content of the blister fluid in one case of burns as 5 Gm per cent. Wells,⁷ in 1925, reported the range as between 4 to 6.5 Gm per cent, while McIver⁸ gave a finding of 3.7 Gm per cent. Both Wells and Pack⁹ commented on this variability, the latter stating "Blister fluid may be an exudate or a transudate, depending upon the degree of irritation. With more intense irritation, the capillary permeability is so altered that the fluid resembles plasma, rather than serum. A clear serum within the blebs becomes cloudy in 24 hours." This clouding, in all probability, is caused by the leukocytic infiltration. In view of the relation of the protein content to the intensity of injury, Cornbleet's¹⁰ attempt to relate the content of blister fluids to the Donnan equilibrium becomes of more academic than practical interest, at least in burns.

It is interesting in this connection that Glenn, Muss, and Dinker¹¹ found that the lymph from the burned extremity of calves is increased not only in the speed of flow, but also in protein contents, by 35 to 75 per cent.

The protein content of the blister fluid, however, is not representative of the protein content of the exudate from burned areas, particularly in late cases. Where extensive tissue destruction has taken place, the separation of the eschar opens up not only the lymphatic channels, but exposes capillaries with different degrees of injury, from which may exude, according to the severity of the injury, any blood element ranging from albumin to whole blood. Where an infection coexists, there is also protein loss from local autolysis and tissue destruction.

The losses per unit area as revealed by polarimetry in the cases of burns are significant. The highest figure was shown by J. W. on the 12th day, when 3.28 mg of nitrogen was lost per sq. cm of surface. At this rate, an average person with 50 per cent of his 1.8 sq. meter of surface involved in burns, could lose 185 Gm of protein in 24 hours, an amount which would deplete the blood almost entirely of its osmotic component.

In view of the constant protein drain, sometimes of enormous magnitude, the difficulty of keeping patients with considerable burnt areas in good protein nutrition, as reported by Taylor, and his group,⁴ is understandable. These authors had recourse to heroic forced feedings, taking considerable trouble and valuable material (plasma and plasma albumin) to keep the cases of severe burns from too severe an emaciation.

When it is realized how much depends upon an effective healing process

in convalescence in burns; and when it is known how the healing process depends upon adequate protein nutrition, the vicious circle introduced by a constant protein drain, with consequent delayed healing, and, therefore, with further protein drain, the importance of the subject can be visualized. This is the more clearly seen if a skin grafting is attempted which further opens up new areas of protein loss, leading to the danger, on the one hand, of inducing shock in a person already hypoproteinemic, and on the other hand, of jeopardizing the taking of such grafts on a malnourished base. What has been said of the relationship between wound healing in burns and the state of nutrition can also be said of the other conditions herein repeated.

In cases of extensive surgical dissection (R. W. and A. G.) it is interesting to note that the losses can run up to almost 59 Gm of protein in 24 hours, equivalent to 644 cc of plasma. This, of course, includes blood. When it is remembered that with this loss outside of the body, there must doubtless be a loss of protein into the traumatized tissues in the area of the dissection, the danger of surgical shock from this cause, alone, is at once apparent. It is, however, reassuring to know that in both of these cases of widespread dissection, the protein loss fell off rather rapidly during the subsequent days.

The case of lung abscess and pyothorax (F. C.) requires some comment. The nitrogen loss of at least 9.57 Gm per day, represents almost all the nitrogen intake in a basic diet and half of the intake in a higher protein diet. In view of this magnitude of nitrogen loss, it is clear why this type of chest cases are so often emaciated and why the mortality rate should be so high.

It may be pertinent in this discussion to bring up a point which is still undeveloped and needs further elaboration. It is the necessity of differentiating between protein loss, which involves protein drain from the entire system, and protein loss, which does not. In the former category may be placed loss of all blood and lymph elements, and to a less degree of urgency, loss of tissues which must be regenerated. In the second category may be placed protein loss involved in losses of parts of the body, such as of the breast in the case of R. W., and of extremities in amputations. Here the actual protein loss involved in the loss of the parts is larger, but since the parts are not to be replaced, it involves comparatively no protein drain to the system. It does not jeopardize health to the extent that a much smaller loss in the first category involves. In fact, it is quite conceivable that the loss of nitrogen from the exuding surface left by the excision of the organ, if it continues could be more detrimental to the body than the large amount lost in the original part. How much of one or the other factor is present in the protein loss in pus and in exudate from infected surfaces is difficult to determine.

It might also be of interest to bring up the question of the adequacy of the civilian hospital diets to support nutrition in cases of large protein drain. The "basic diet" or "standard diet" recommended by the National Research Council, on the basis of Sherman's¹² survey, in 1920, contains 70 Gm per kilo-

gram of body weight, or 11.2 Gm of nitrogen. Recommended as a maintenance diet, it has been adopted generally as a basic hospital diet. Since this diet is supposed to provide a margin of safety of from 50 to 100 per cent, it may be assumed that the minimum nitrogen requirement has been placed by Sherman as from 5.6 to 7.5 Gm per person, giving a margin of safety of 3.7 to 5.6 Gm. The nitrogen loss in most of the 13 cases in Table I is larger than this margin at some stage of the convalescence, and for this reason, this diet is inadequate for this type of case. This inadequacy becomes evident when one remembers that this gram-for-gram matching has left out of consideration that the loss of urinary nitrogen is markedly increased in a large number of disease conditions of this type, and that it takes more than one gram of ingested nitrogen to cover one gram of nitrogen lost from the body.

The "high protein" diet consists of from 120 to 130 Gm of protein (19 to 21 Gm of nitrogen), and should be adequate to replace moderate amounts of protein drain, provided pain, anorexia and other upsets do not reduce this intake. In patients with extra metabolic protein drains of above 5 Gm per day, even this higher protein diet may not be adequate.

Two practical implications of the foregoing discussion may be set forth. The first, applicable to the civilian hospital, is that the protein content of the "basic diet" should be increased in order to provide for a larger margin for the replacement of increased nitrogen loss in disease—offhand, a 50 per cent increase would not be too much. The second, applicable to the practicing physician, is that he develop an awareness for not only the vitamin, but, also, for the caloric and nitrogen needs of the patient particularly in conditions which involve large losses of proteinous body fluids, and that he familiarize himself with the methods of special alimentation now available, namely, the use of amino-acid mixtures orally or parenterally. If natural alimentation fails, these measures may be of critical value. Plasma transfusions, generally speaking, should now be reserved for more emergent uses, such as correction of an acute hypovolemia.

Mention has been made of the advantages of introducing precise surface measurements into this study. This greater degree of precision may throw light on the following points:

- 1 The relation between the rapidity of healing or contraction of the lesion, and the general protein nutrition of the patient
- 2 The differences in the amount of protein loss associated with the different tissue planes involved
- 3 Evolution of the amount of exudation as the lesion ages
- 4 Determination of whether different types of infectants excite different rates of protein loss
- 5 The effect of local therapeutic measures on the amount of exudation

However, it is to be remembered that the determination of the area of

skin involved in a burn is not necessarily the same as the absolute area available for exudation, any more than is the measurable area of the intestinal mucosal surface the same as that offered by the villi for absorption. In the case of the burned area, the crypts and folds and other irregularities in the denuded surface may be roughly compared with the intestinal villi in multiplying the effective absorbing surface.

Finally, it is to be mentioned that the above study is a random one. A more complete study, involving a continuous record, not only of the nitrogen loss in the exudates, but also in the urine and feces, is indicated. The method devised by Hirschfeld, and his group,² and modified to throw light on the above points, may well serve as a pattern.

SUMMARY

1 The exudate of 13 surgical cases, representing four surgical conditions, were analyzed for nitrogen contents.

2 The nitrogen losses were, in some cases, of sufficient magnitude to jeopardize recovery.

3 The significance of such losses, and the indications for a more exhaustive study were discussed.

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THE EFFECTS OF TEMPERATURE ON THE DIGESTION OF COLLAGEN SUTURES AND SURGICAL GUT (CATGUT) BY ENZYMES AND BY THE SUBCUTANEOUS TISSUES OF THE FROG*

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NATIVE COLLAGEN FIBERS from the skin or tendons are extremely resistant to enzymes, but when mechanically comminuted to very small particles or heated they become fairly readily digested by enzymes (Sizer¹) Relatively resistant acid-swollen beef tendons can be macerated into dilute suspensions (though the collagen may not pass through filter paper) and subsequently reprecipitated to reform fibers of similar ultrastructure to the original (Schmitt, *et al*,² and Bear^{3 4}) Such treatment renders them relatively digestible by many different animal and plant enzymes Similarly, the fibers are digested and absorbed after implantation in the animal body, and the available evidence suggests that this action is brought about by enzymes liberated from white blood cells

The effects of temperature upon the digestion of collagen have been studied in a qualitative manner mostly by leather chemists interested in the action of enzymes during the bating of hides (cf Wilson⁵) Using crude collagen preparations in the form of hide powder, Thomas and Seymour-Jones⁶ reported that appreciable solution by trypsin occurred at 40° C but was very slight at 23° C Similarly, Merrill⁷ studied the action of trypsin on hide powder by measuring the increase in soluble nitrogen during digestion, and his data indicate a threefold increase in rate from 15° C to 25° C, a nineteen-fold increase from 25° C to 35° C, and a sixfold increase from 35° C to 45° C On theoretical grounds, however, the digestion of collagen by trypsin might be expected to increase exponentially with temperature in accordance with the Arrhenius' equation (for a review cf Sizer⁸), since this is the case for the action of trypsin on several different proteins (Butler,⁹ and Sizer

$$* \mu = \frac{4.6 (\log k_2 - \log k_1)}{1/T_1 - 1/T_2}$$

and Josephson¹⁰) The present work was undertaken with the purpose of studying quantitatively the action of proteases on collagen as a function of temperature and comparing these results with those on the digestion of collagen implanted in the subcutaneous tissues of the frog

* This work was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Massachusetts Institute of Technology

METHODS

The collagen used in these studies was either in the form of collagen sutures or plain commercial surgical gut sutures (size No 0000) prepared from sheep gut. The digestion of collagen or catgut sutures by enzymes has been studied by the method of Jenkins and Hrdina,¹¹ as modified by Lion and Sizer.¹² It consists in attaching a two-gram lead weight to the suture and immersing the suture in a test tube of enzyme solution incubated in a water bath with a temperature control of $\pm 0.05^{\circ}\text{C}$. The free end of the fiber is connected to a telephone message counter driven by an electric clock. When the suture is digested the lead sinker falls, a circuit is broken, and the digestion time in minutes may be read directly from the counter. A few drops of toluene are added to the enzyme solution to prevent bacterial growth. The pepsin solutions at $p_{\text{H}} 2.0$ contained 0.1 per cent concentrated HCl, while the other enzyme solutions were not buffered and the p_{H} was about 7.

For the animal experiments medium-sized winter frogs were used. The sutures were implanted subcutaneously, after ether anesthesia, by lifting up a fold of the abdominal skin and passing through it a suture threaded to a surgeon's straight needle. One of the free ends of the suture is slipped beneath the skin, while the other is tied to the skin with surgical silk at the point of insertion. Three sutures were implanted in each frog and, at successive intervals, samples were withdrawn. The extent of digestion was measured by determining the breaking strength of the washed and dried fiber as compared with the original sample before implantation. During the course of the experiment the frog was kept in a cage which was immersed in a constant temperature water bath. Although the frog could move about in the cage, it was impossible for it to lift its abdomen, containing the sutures, out of the water.

A DIGESTION OF COLLAGEN AND CATGUT SUTURES BY TRYPSIN AND PEPSIN

Using the weighted fiber-breaking time technic, the digestion of sutures has been studied over the temperature range from 1° to 60°C . When log rate is plotted against the reciprocal of the absolute temperature (Fig 1) the points fit along a straight line up to 45°C , above which the points fall from the line due to temperature inactivation (denaturation) of the enzyme. The slope of the line corresponds to an activation energy of 31,000 cal per Gm mole* for both pepsin and trypsin. It is very surprising that the same activation energy characterizes the action of both pepsin and trypsin on collagen, since the activation energy usually is different for each enzyme (Sizer⁸). In accordance with results on other enzymes the activation energy is independent of the purity of the enzyme, since the same value is obtained

* "Mole" is defined as "the weight in grams equal to the molecular weight" (*Chemical Handbook*)

(Fig 1) for 10 per cent crude trypsin (Cenco) partially purified trypsin (Cenco, purified by using only the aqueous filtrate) and also in preliminary experiments with crystalline trypsin (Lehn and Fink). Similarly, the same values characterize crude 10 per cent (Cenco) and crystalline 0.1 per cent (Lehn and Fink) pepsin†. The activation energy is also independent of the

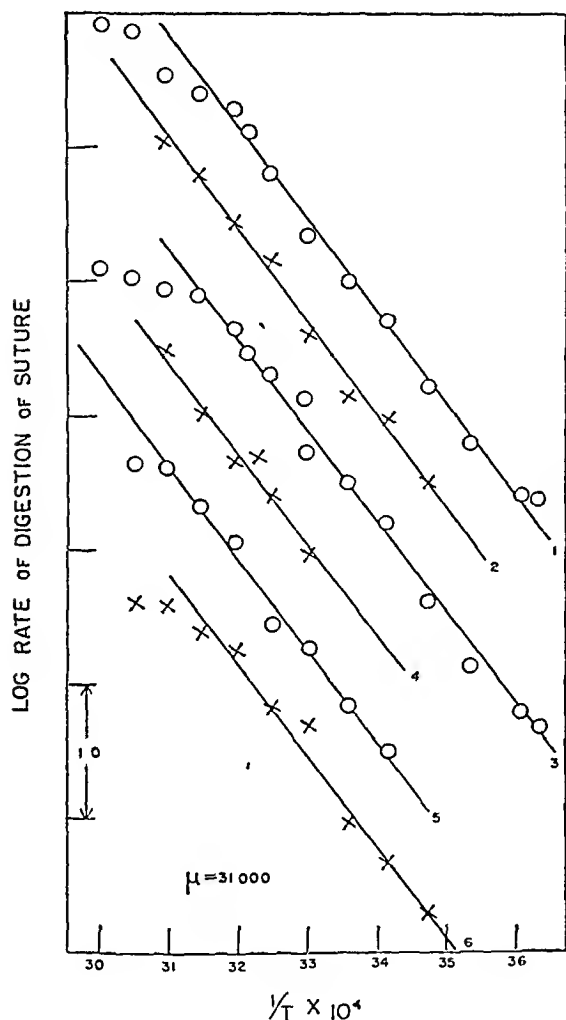


FIG 1—Log rate of digestion of collagen and catgut sutures in enzyme solutions is plotted against $1/T$. The same activation energy of 31,000 cal per Gm mole is obtained in all cases

- 1 Collagen sutures in 10% crude trypsin
- 2 Collagen sutures in filtered 10% trypsin
- 3 Collagen sutures in 10% crude pepsin
- 4 Collagen sutures in 1% crystalline pepsin
- 5 Catgut sutures in 10% crude trypsin
- 6 Catgut sutures in 10% crude pepsin

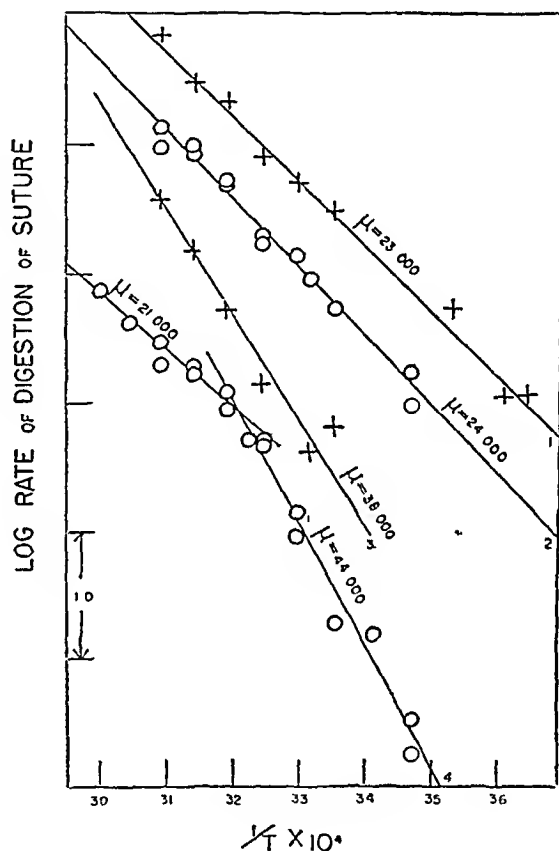


FIG 2—Log rate of digestion of collagen sutures in enzyme solutions is plotted against $1/T$

- 1 0.1% crystalline chymotrypsin, $\mu = 23,000$ cal
- 2 1% orthozyme, $\mu = 24,000$ cal
- 3 1% keralin, $\mu = 38,000$ cal
- 4 1% papain, $\mu = 21,000$ above and 44,000 cal below 38°C

source and purity of the collagen, for the same activation energy is obtained with collagen fibers (either mono- or multifilament) from relatively pure collagen of beef tendon and plain catgut sutures from relatively crude collagen of sheep intestine

† In occasional experiments with both crystalline trypsin and pepsin an activation energy of 22,000 cal per Gm mole instead of 31,000 cal is obtained, but the reason for this is not known

B DIGESTION OF COLLAGEN SUTURES BY OTHER ENZYMES

Since the same activation energy characterizes both the pepsin- and trypsin-collagen systems, it is important to know whether the same value will be obtained for other enzymes. As indicated in Figure 2 the activation energies of the collagen-enzyme system are 38,000 cal with 1 per cent

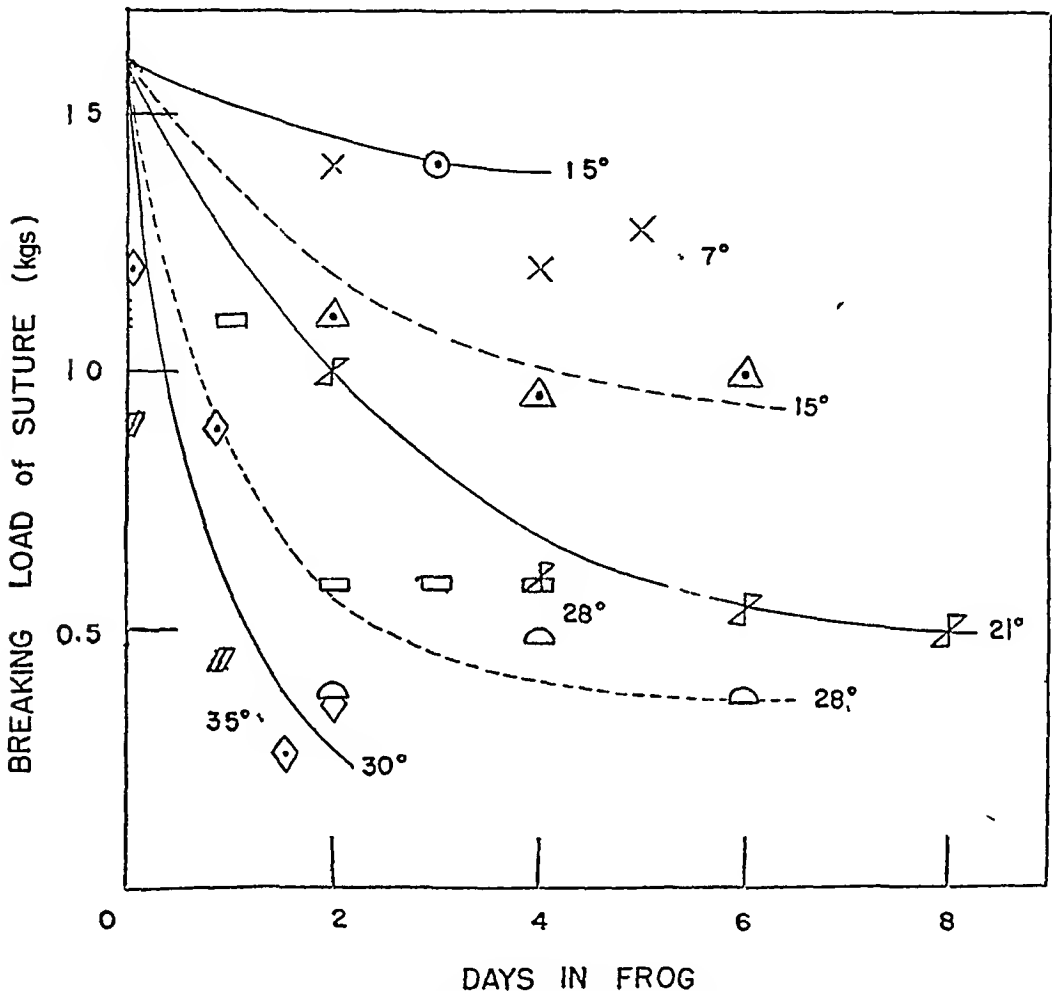


FIG 3—The strength (Kg breaking load) of collagen sutures is plotted against the number of days the suture has remained in the subcutaneous tissues of frogs, which were kept at different temperatures during the experiment

kealain (American cyanamid), 24,000 cal with 1 per cent orthozyme (Rohm and Haas), 23,000 cal with 0.1 per cent crystalline chymotrypsin (Lehn and Fink), and 21,000 cal above and 44,000 cal below 38° C with 1 per cent papain (Merck). The results with papain are especially interesting, for it is the only known enzyme which will (although very slowly) attack native, unswollen collagen fibers. The enzyme is relatively heat stable even up to 60° C, and the papain-collagen system is characterized by one activation energy above 38° C and another below this temperature (for similar enzyme systems, see Sizer⁸). From these experiments with several different proteases it appears that, in general, as would be expected, the activation energy

for the digestion of collagen is characteristic of the specific proteolytic enzyme used. The significance of the identity of the value for pepsin and trypsin is not known. Whether or not it is merely a coincidence must await further studies with these enzymes. The activation energy for both enzymes is different from the values reported for their action on other proteins (Butler,⁹ Sizer and Josephson,¹⁰ and Sizer⁸).

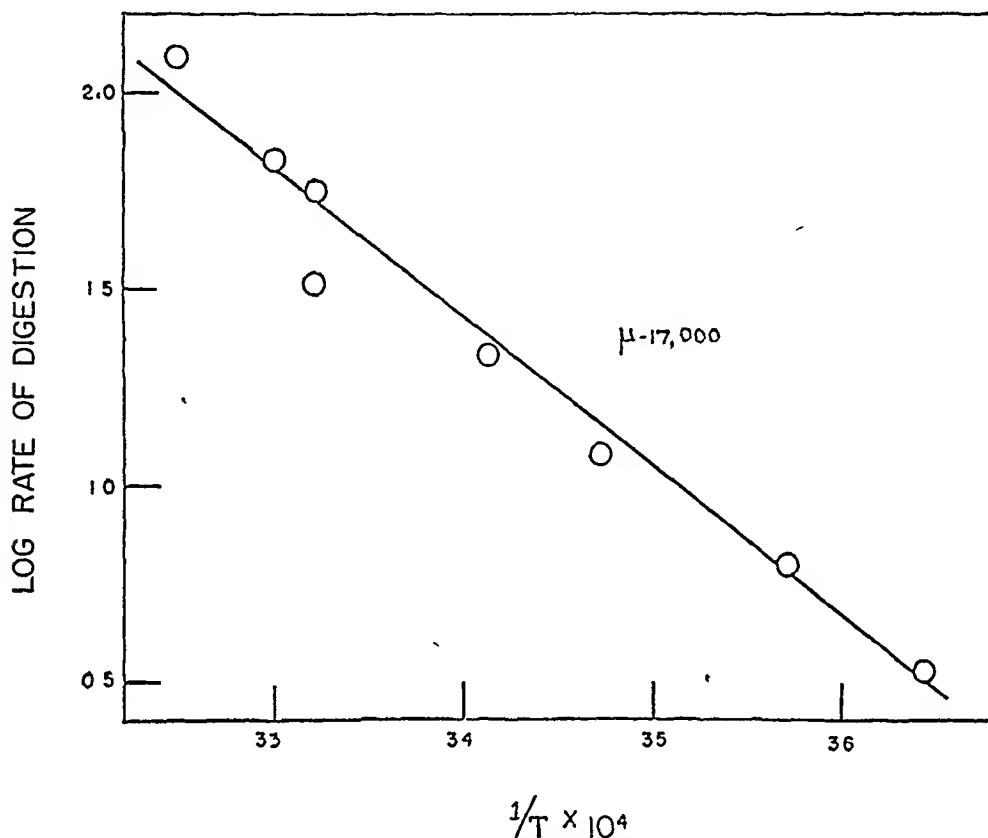


FIG. 4.—Log rate of digestion of collagen sutures implanted subcutaneously in the frog is plotted against $1/T$. The rate of digestion was taken as ten times the reciprocal of the time in days after implantation required to reduce the strength of the suture from 16 to 1.4 Kg. This was calculated from the curves of Figure 4.

C DIGESTION OF COLLAGEN SUTURES IN THE FROG

The digestion and disappearance of absorbable sutures implanted in animals appears to be due to the action of tissue enzymes. Since the influence of temperature on the action of certain enzymes *in vivo* and *in vitro* appears to be the same (cf. Sizer⁸), it might be expected that the rate of digestion of the sutures would also increase exponentially with temperature in accordance with the Arrhenius' equation. From an experimental point of view the most convenient poikilothermic animal is the frog, but results which might be obtained do not necessarily depict the situation which would exist in mammals and particularly man. The winter frogs used in these experiments had been kept for several months in the laboratory without food before use. After implantation for several days many fibers broke at the point of entry through the skin instead of pulling out readily. It then became necessary to expose the suture by cutting open the skin. After the

removal of the suture, the incision in the skin was closed with surgical silk. The sutures after removal were washed and dried before testing for strength by measuring the breaking load.

When breaking load (Kg) is plotted against implantation time in days (Fig. 3) it is apparent that at each temperature the strength of the suture decreases in a smooth hyperbolic fashion much the same as in rabbits* and in dogs (Jenkins and Hrdina¹³). The plotted points are quite scattered due to the many experimental difficulties encountered in this type of experiment. Rate may be calculated from the reciprocal of the time required to produce a given reduction in strength of the suture, *e g*, to reduce the breaking load from 16 to 14 Kg. The log of the rate of digestion ($\log 10/\text{time in days for the reduction in strength}$) is plotted against $1/T$ in Figure 4. The digestion of sutures implanted subcutaneously in the frog increases exponentially with temperature in accordance with the Arrhenius' equation just as does the digestion of sutures by enzymes. The activation energy of 17,000 cal per Gm mole for the digestion of sutures in the frog is different, however, from that encountered with any of the particular enzymes which have been studied. Histologic evidence suggests that the digestion of sutures implanted in animal tissues is brought about chiefly by leukocytes (Jenkins, *et al*¹⁴). Experiments on the action of human and beef blood on the digestion of collagen sutures indicate that blood enzymes do attack the sutures. Fractionation by centrifugation of beef blood shows that most of the proteolytic action of blood is associated with the leukocytes rather than with the plasma or red blood cells. It has not yet been possible to obtain a stable preparation of proteases from leukocytes, in order to determine whether or not the activation energy for the digestion of collagen sutures by leukocytic enzymes *in vitro* is the same as that for the digestion of the sutures implanted in the tissues of the organism.

It seems significant that the digestion of collagen sutures both *in vivo* and *in vitro* increases exponentially with temperature, but since the enzymes studied are probably not the same as the ones which digest the suture in the tissue the activation energies are correspondingly different. One practical aspect of this study lies in the possible application of the results to problems of human surgery. An important problem involved in the use of catgut sutures lies in digestion of the suture before healing is completed, with the resulting opening up of the wound. It is apparent from this work on collagen and catgut (only preliminary catgut experiments have been performed with the frog) that an important factor determining the rate of digestion and absorption of sutures is the body temperature. In a patient an increased temperature of 4° C might be expected to produce a 100 per cent increase in the rate at which absorbable sutures are destroyed in the incision if the human enzymes (or bacterial enzymes in the case of infected wounds) behave like trypsin or pepsin. If the human situation is similar to that in the frog

* Unpublished experiments by Sizer and Gould

a rise in temperature of 7°C will produce a doubling in the rate of destruction of the suture. In either situation, it is apparent that any elevation in body temperature may produce a marked increase in the rate of absorption of the suture. Less extensive experiments with tanned sutures (either collagen or surgical gut) indicate temperature effects on digestion similar to those for the plain sutures.

SUMMARY

The digestion of sutures of beef tendon collagen and of surgical gut by trypsin or pepsin increases in rate with temperature in accordance with the Arrhenius' equation with an activation energy of 31,000 cal per Gm mole. The activation energy is independent of the source and treatment of the collagen and is also independent of the purity of the enzyme preparation.

When collagen sutures are digested by other enzymes the activation energy is characteristic of the collagen-enzyme system. The activation energies are 38,000 cal with kernalin, 24,000 cal with orthozyme, 23,000 with chymotrypsin, and 21,000 cal above and 44,000 cal below 38°C with papain.

When collagen sutures are implanted subcutaneously in frogs, the rate of digestion, as measured by the rate of loss in tensile strength, increases exponentially with the absolute temperature of the frog. The activation energy is 17,000 cal per Gm mole. It is suggested that this value is the activation energy of the proteolytic enzyme, presumably from the white blood cells, which is responsible for the digestion of sutures in the subcutaneous tissues. It is pointed out that suture absorption in man may be greatly accelerated by postoperative fever.

The author is indebted to Doctors D. F. Waugh, T. P. Salo, and E. L. Duggan, of the Collagen Research Group at the Massachusetts Institute of Technology, for supplying the collagen fibers and for advice in the present investigation.

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THE SUBMUCOSAL MORCELLATION OF HEMORRHOIDS

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LT H W AHRENBERGER, M C -V(S), U S N R

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BECAUSE NEARLY EVERYONE has hemorrhoids in one form or another and because complications of hemorrhoids and hemorrhoidectomies may be very distressing, oftentimes disabling, we would like to present our preoperative, new surgical technic and postoperative care for your consideration, especially since we are aware of the fact that the methods employed in the early 1800's by the French Surgeons are still in use ¹

Hemorrhoids may occur because of straining at stool, they may follow pregnancy and they are also found in men who suffer from chronic coughs or from prostatic hypertrophy. Another cause of venous stasis is an infiltrating carcinoma of the rectum causing partial obstruction. It is, therefore, important to make a complete physical examination on all patients who present themselves for hemorrhoidal surgery. Since the present war we have seen many young men develop hemorrhoids because of altered diet, nervous tension and lack of proper toilet facilities. It was found that many of the marines and sailors became so afflicted while at the actual battle front. At one station the surgical staff averaged 3-4 hemorrhoidectomies per week, and these on boys in the 17-21 age-group.

Considering that hemorrhoids, either internal or external, are in truth "varicose veins of the rectal area" it is difficult to condone the present-day practice of "clamp and excision." The disease, being one of blood vessels primarily, there is no need for the surgeon to sacrifice large amounts of the rectal mucosa, underlying connective tissue and even muscle. An apt analogy would be to have the surgeon, who, in attempting to cure the patient of varicosities of the lower extremity, merely clamped across the varix, and excised skin, muscle and even nerves.

The present status of hemorrhoidectomy is much the same when so much healthy and uninvolved tissue is sacrificed in order to get at the offending vein. With the removal of such a large block of mucous membrane and adjacent tissue in hemorrhoidectomy, one can, without difficulty, readily explain its complications, namely, stenoses, loss of sphincter control, fissures, abscesses, not to mention pruritus and pain seen in almost every hemorrhoidectomized patient. It is altogether too common that the hemorrhoid patient dreads his operation only because he has been told about the pain and distress suffered by other patients.

Thus, realizing all this, we have attempted to correlate a technic of hemorrhoidectomy which is along anatomic lines and which attempts to preserve a normally functioning rectal tube. The result has been that the

common sequelae of hemorrhoidectomy have been reduced to a minimum and the operation itself surprisingly simplified

Injudicious removal of tissue containing nerve filaments or even vigorous dilatation of the anus is sufficient to so harm the structures supplied by these nerves that incontinency of sphincter, proctitis, pain, and delayed healing may occur

Therefore, considering anatomic principles, the following method of obliteration of hemorrhoids has been devised by one of the authors (H B B)

Adequate preoperative preparation of the hemorrhoid patient is as important as in any other surgical procedure and contributes directly to satisfactory results, a fact which is many times overlooked. The patient is usually hospitalized the night before, having had previously a thorough physical examination and, may we stress, a complete history. Conditions predisposing to hemorrhoids are especially sought after, such as abdominal tumors, chronic bronchitis, cirrhosis of the liver, *etc*. Special examination for carcinoma must always be made prior to operation. Dr Charles Mayo said "I could win the office of President of the United States on the platform of free finger cots for doctors to do rectals." It is our custom to give the patient a sedative the night before, consisting of a barbiturate to allay any apprehension he might have. The perineum and anus are prepared, and three hours preoperatively the patient receives a soap-suds enema which is followed by a saline colon irrigation to remove any of the irritating qualities of the soap. A light breakfast may be given. We have found that a repetition of the barbiturate is usually sufficient as an immediate preoperative medication, however, the more apprehensive and nervous patients do require sedation with morphine and scopolamin combinations. The patient's general condition and mental make-up are the determining factors.

The anesthetic of choice is caudal block. This is given 20 to 30 minutes before the operation is to be performed. The technic employed is one commonly described, either 1 per cent novocaine or 1 per cent metycaine may be used, 30-35 cc of solution is usually sufficient to insure adequate anal anesthesia. Local infiltration of these solutions has also been utilized with surprisingly good results.

The patient is then ready for operation. Two positions have been used, the lithotomy or Boue, depending on the operator's choice. Thereafter, the anal area is widely prepared in the usual manner, tincture of merthiolate usually being employed, and then draped with sterile sheets. First and foremost, a careful proctoscopic examination is routinely carried out to visualize the anal canal and to inspect for the possibility of malignancy. This is best done now because of the anesthesia. At the same time, any residual foreign matter may be removed. A vigorous anal dilation is never done. It is felt that this is not necessary and may even be harmful. Many bothersome post-operative sequelae have thus been eliminated by refraining from this stretching.

No evidence of carcinoma having been found, each hemorrhoidal tag is next identified. A small linear incision, perpendicular to the axis of the

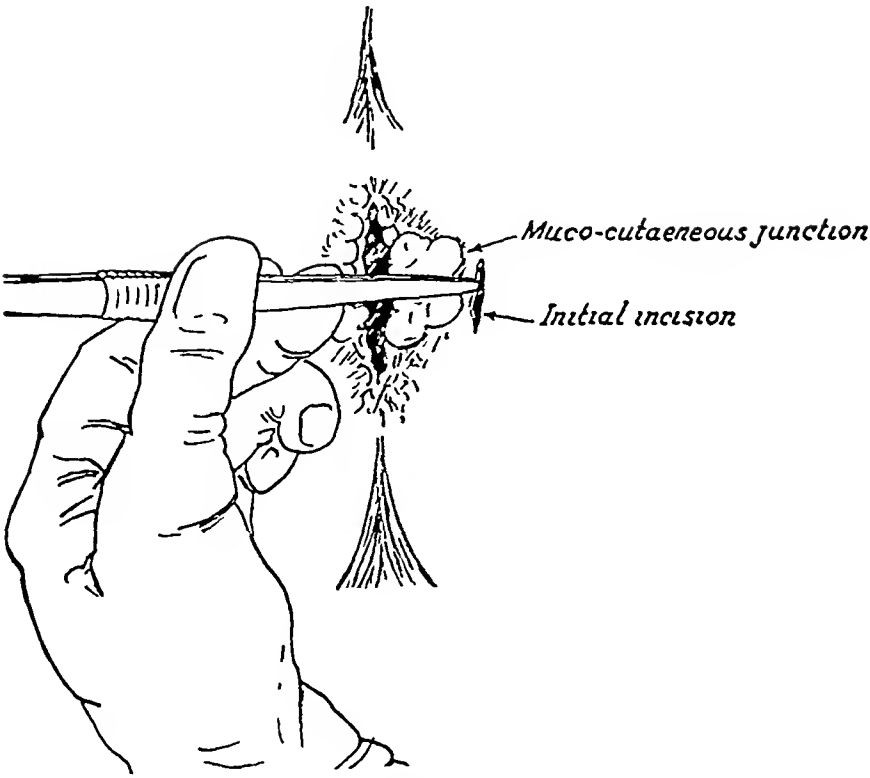


FIG 1

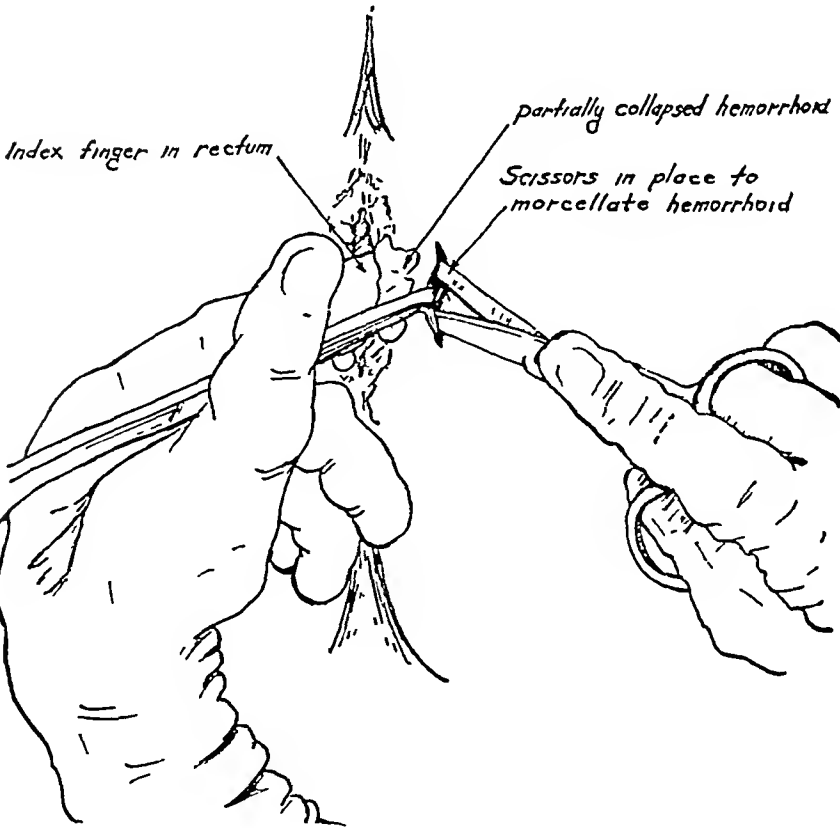


FIG 2

rectum, is made with the knife in the skin approximately 3 cm from the base of the first external hemorrhoid. This incision is usually just outside the pigmented area which surrounds the anus or approximately 1.5 cm from

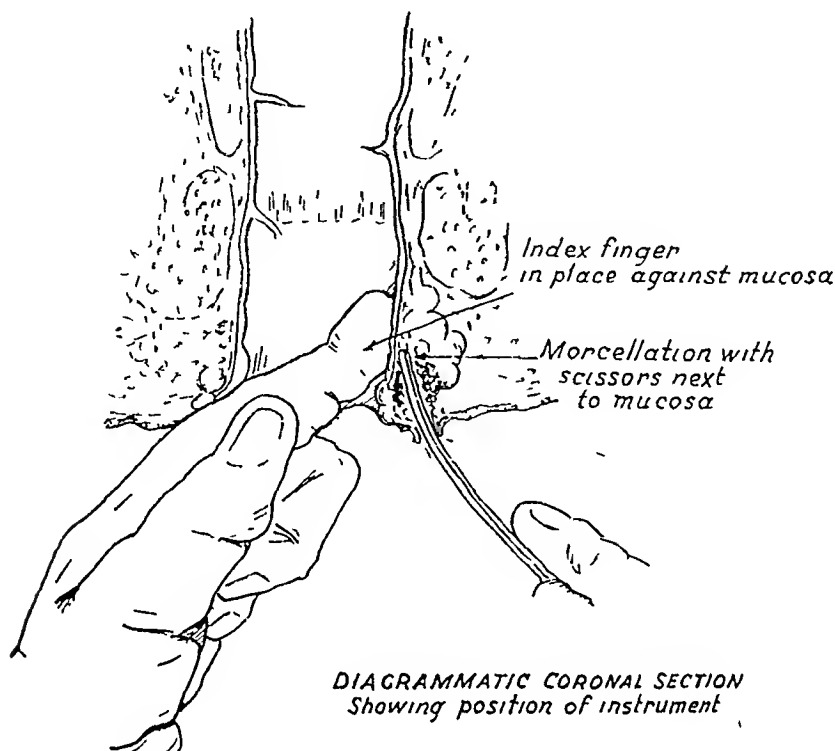


FIG 3

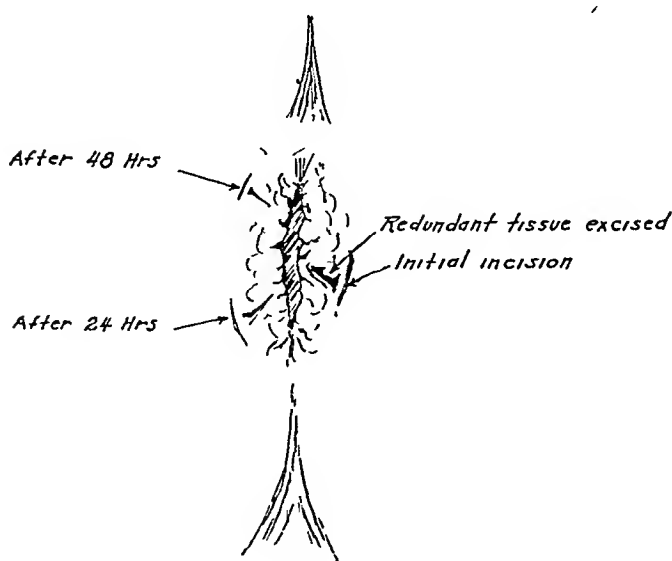


FIG 4—Composite sketch showing healing stages

the mucocutaneous border (Fig 1). Next, the medial edge of the incised skin is grasped with an Allis forceps. Holding the forceps up on the hand, the mucous membrane is dissected free from the hemorrhoid with Mayo

scissors (both points dull) (Fig 2) The dissection is then carried in like manner upwards, using the finger in the rectum as a guide until Hilton's line is reached (Fig 3) This accomplished, the entire diseased hemorrhoidal vessel is morcellated by short bites with the scissors If clots are present, they are removed After complete careful morcellation, the scissors are withdrawn and any redundant, excessive mucous membrane is removed by a "V"-shaped excision (Fig 4) It must be remembered, however, that much of this redundancy will be reduced in the process of healing A similar procedure is carried out on the remaining hemorrhoidal tags Thereafter, at the

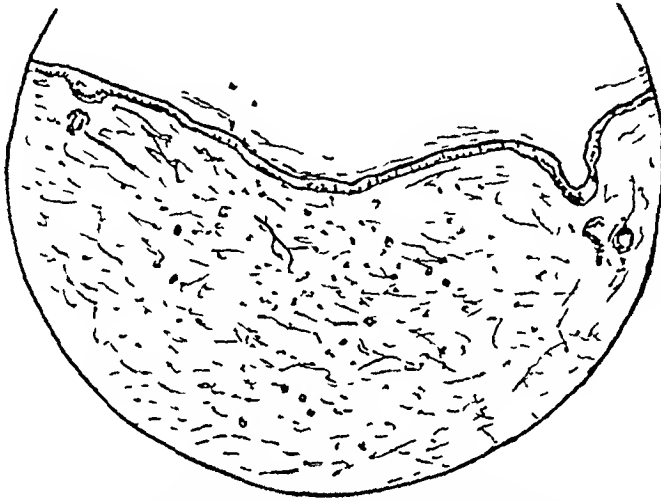


FIG 5—Experimental section showing intact mucosa over operated area (72 hours postoperative)

discretion of the operator, a nupercaine-gauze pack may be inserted for hemostasis

Scrulpous attention is also paid to the patient following the operation On the following morning the nupercaine gauze, if inserted, should be removed If the patient is unable to void in 12 hours, postoperative catheterization is carried out Hot witch hazel packs have been found to be very beneficial and these applications should be started the evening of the operation To be effective these packs must be hot A cold and clammy pack can be very uncomfortable Mineral oil, ounces one, by mouth, is given three times a day, fluids are given freely, with a light diet Hot sitz baths are instituted on the third day^{2,3}

The operation being technically so simple, its contraindications are few Of course, seriously debilitating disease is always investigated and no operative procedure should be carried out in such an instance A large ulcerated mucosa would make the dissection of the mucous membrane impossible and, thus, the operation impracticable, since its continuity could not be preserved Thrombosis without ulceration, however, is no contraindication

In 34 consecutive hemorrhoidectomies treated by this technic, three points were outstanding (1) Not one of these patients complained of undue pain or discomfort either during the operation or after it The enema given on the third postoperative day was easily accomplished and normal bowel movements followed, the patients being allowed to go to the toilet (2) Not one of

these patients suffered distention gas pains, or had to be catheterized. Normal bowel and bladder physiology was almost uninterrupted before and after the operation. (3) The speed of recovery was rapid. Two-thirds of these patients were up and about on the third postoperative day. At the end of one week complete healing had occurred in all and in most it was difficult to ascertain that the patient had had hemorrhoids. Postoperative scars or stenoses were not discernible. Five cases were encountered in which bleeding necessitated the use of rectal pack. The remainder required no packing and frequent examinations of the dressing showed only slight oozing.

In comparing our results with those of the clamp and excision or clamp and cautery methods, we are impressed by the fact that our results showed an absence of discomfort and pain, which made for a much quicker recovery and shorter convalescence. The fact that practically negligible inhibition of urination was found in these patients also was gratifying. The operation itself is anatomically fool-proof, insofar as the sphincter is not invaded, and the anal canal is not forcibly dilated either during or after. The operation not being a technically difficult one, it is relatively safe. The postoperative complications are at a minimum, and the diseased vein is completely obliterated, thus, curing the patient. The patient is further pleased at the reduction of hospitalization and the rapidity with which he is back at work. This operation was developed three years ago and, so far, we have had no recurrences in any of our cases. The patient is visibly as well as clinically cured, and has no complaints, after this type of surgical intervention.

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ALBRIGHT'S SYNDROME

REPORT OF A CASE ASSOCIATED WITH MULTIPLE PATHOLOGIC FRACTURES,
DISSEMINATED FIBROUS DYSPLASIA OF BONES, PRECOCIOUS
PUBERTY AND MULTIPLE PIGMENTED NEVI

LT COL ALBERT BEHREND, M C ,

IN 1937, Albright,¹ and his associates, called attention to a group of cases in which the symptoms were sufficiently uniform to warrant their classification as a syndrome. While individual cases had been described sporadically by various authors prior to 1937, attention became focused on them as a clinical entity by the report of Albright, so that the syndrome now bears his name.

The original article by Albright noted the following characteristic findings:

(a) Bone lesions which have a marked tendency to be unilateral and which show osteitis fibrosa on histologic examination.

(b) Brown, nonelevated pigmented areas of the skin, which tend to be on the same side as the bone lesions.

(c) An endocrine dysfunction which in females is associated with precocious puberty.

The following case fulfills all the requisites noted above and is presented in the belief that it is the thirty-fifth case to be reported in the literature. In addition to these, Gorham, and his coworkers,² list so-called "partial" cases which show some but not all of the characteristic findings. The disease remains an interesting medical curiosity since the etiology is still obscure and there is no specific therapy.



Case Report—G F, white female, age seven, was first seen at the Station Hospital on June 25, 1942. On June 24, 1942, she fell from her tricycle and noted pain in the right thigh which was not, however, severe. She walked into the house, but the following day was unable to bear weight on the right leg. The parents noticed some deformity of the right thigh, and she was brought to the hospital.

FIG 1—Demonstrating multiple hyperpigmented areas in the skin.

On admission, the patient was found to be an exceptionally intelligent and co-operative child, well developed, but with no precocious secondary sex characteristics. There were multiple small areas of dark pigmentation on the trunk (Fig 1) and extremities, which, at the time, were not considered of unusual significance. External rotation of the right foot and ankle, with anterior bowing of the thigh, were noted, and the right leg was slightly shorter than the left. There was pain in the upper third of the femur on rotation of the leg. Roentgenologic examination disclosed a comminuted intertrochanteric fracture of the right femur. Subsequent review of the original films at the time of the second admission showed that the fracture was a pathologic one in a region of cystic bone, but this fact was not at first appreciated.



FIG 2—Note precocious development of secondary sex characteristics. Age Eight years

On June 25, 1942, under open-drop ether anesthesia the fracture of the femur was reduced on the Hawley table and a Whitman spica of plaster of paris was applied. An excellent reduction was obtained and maintained for three months, after which the encasement was removed and weight-bearing was begun. Shortly thereafter the family moved to another post.

Second Admission—The child was apparently well until July 10, 1943. On that date, while walking downstairs, she twisted her leg and fell. Pain in the right thigh was noted at once. Roentgenologic examination elsewhere showed marked deformity of the right hip and thigh, and there was a large bone-cyst in the subtrochanteric region, with an incomplete fracture line in the lateral wall of the cyst. Films of the lower legs showed cystic areas in the upper third of both tibiae. Films of the skull and other bones were normal.

She was readmitted to the Station Hospital on July 12, 1943. Roentgenographic findings as noted above were confirmed. Since the fracture was incomplete, and there was no shortening, a splint was not applied, but the patient was confined to bed until August 31, 1943. At this time, the fracture line had entirely disappeared, but the cystic area of bone showed little change. She

was allowed to return to her home, and it was recommended that she stay in bed for four more weeks.

Laboratory Data—Kahn—negative. Routine urinalysis normal. Red blood cells 4,110,000, hemoglobin 90 per cent. White blood cells 8,500, polymorphonuclears 55 per cent, lymphocytes 44 per cent, eosinophils 1 per cent. Serum calcium 11.5 mg and 10.4 mg per 100 cc. Serum phosphorus 5.8 mg and 5.4 mg per 100 cc. Phosphatase 9.2 modified units. Urine calcium 284.4 mg per vol of 775 cc. Urine phosphorus 740 mg per vol of 775 cc (24-hour specimen).

Third Admission—The patient was readmitted to the Station Hospital October 25, 1943. Roentgenograms taken elsewhere showed increase in the area of cystic bone in upper right femur. At this time, enlargement of the breasts first became evident (Fig 2). Also, during this admission, the patient menstruated for a period of three days.

Questioning revealed that menstruation had occurred first at the age of three and again at the age of seven. This was the third episode of vaginal bleeding. Because of the increasing size of the bone cyst of the femur, operation was advised, and performed November 1, 1943.

Operation—Under ether anesthesia, the right femur was exposed in the region of the great trochanter. The periosteum appeared normal but the underlying bone was pitted. The thin cyst wall was readily unroofed with a chisel and mallet. The cyst cavity was curetted. It contained fine bony spicules that formed a lacy network in



FIG 3—Roentgenogram showing condition of right femur at time of discharge from hospital. This leg was the site of three (3) fractures, and operation consisted of curettement of cyst and insertion of bone chips.

the cyst, and bled very freely. Multiple bone chips were taken from the shaft of the distal portion of the femur and placed in the cyst cavity. A transfusion of 250 cc of whole blood was given during the operation.

Convalescence was uneventful until November 13, 1943, when the patient fell out of bed while asleep. Roentgenologic examination showed a complete fracture of the right femur through the region of the bone cyst, with marked angulation. On November 16, 1943, Russell traction was applied, but this had to be removed on November 19, 1943, because large blisters had developed beneath the traction tapes. On November 22, 1943, under local anesthesia, a Kirschner wire was inserted, in the supracondylar region of the right femur, and traction was applied with the leg on a Thomas splint with a Pierson attachment. The Kirschner wire was removed January 17, 1944. At this time, there was good callus at the site of the fracture and the cystic area in the bone appeared more homogeneous.

On January 17, 1944, aluminum acetate therapy was begun on the advice of Dr. Ralph K. Ghormley. This was continued until February 23, 1944, when she was dis-

charged from the hospital. At this time, the patient was sitting up in a chair but no weight-bearing was permitted.

A specimen of bone removed from the cyst at operation was forwarded for examination, but was lost in transit.

Fourth Admission—The patient returned to the Station Hospital April 2, 1944. Her condition, in general, was good. She had not menstruated since the last admission. Her height was 60 $\frac{3}{4}$ inches and she weighed 111 pounds (50.5 Kg). Neurologic examination was normal. Complete body roentgenograms were made at this time—the first time that this had been done since her second admission in July, 1943. The cystic area in the right femur, the site of three fractures, showed little change from

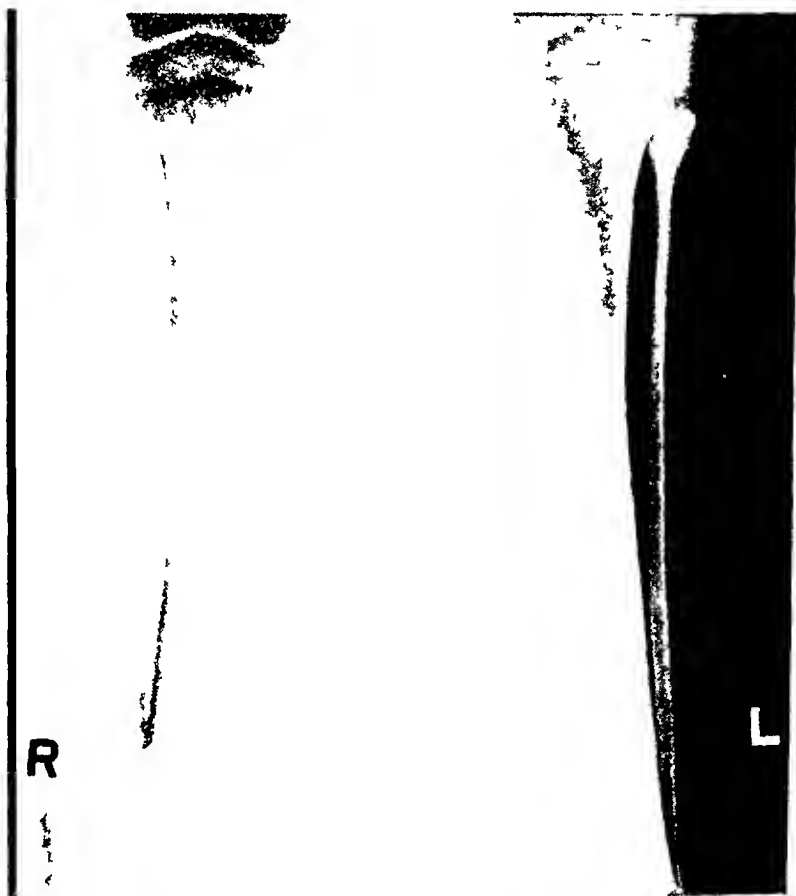


FIG. 4—Roentgenogram of right and left legs showing cystic changes in the upper third of both tibiae and right fibula.

the previous examination in January 1944.³ The bones of the skull, including the sella turcica, appeared normal. The cystic area in the left tibia appeared to be enlarging.⁴ In addition to the right femur and left tibia, the following bones showed minor degrees of cystic change, all notably on the right side, namely, fibula, tibia, ischium, ilium, humerus, 1st metatarsal, and 3rd and 4th metacarpal (Fig. 5). The cysts involving the fibula, ischium, ilium, humerus, metatarsal and metacarpals appear to have developed since the time of the second admission—indicating progression of the disease.

Laboratory Data Urine normal. No Bence-Jones protein present. White blood cells 7000, polymorphonuclears 68 per cent, lymphocytes 32 per cent. Red blood cells 3,770,000, hemoglobin 80 per cent. Blood cholesterol 163, phosphorus 3.5, serum calcium 9.5, and phosphatase 12.3.

Aluminum acetate therapy was again instituted on admission. On April 4, 1944, operation was carried out on the left tibia, under light sodium pentothal intravenous anesthesia. The periosteum overlying the tibia appeared thickened and a specimen was removed for biopsy. On separating the periosteum over the cystic bone, it was noted that the cortex was already disrupted. The cyst cavity was readily unroofed with a sharp curette. The contents of this cyst was in marked contrast to that in the femur. It was soft, yellow, homogeneous and wax-like. A specimen was removed for biopsy. Bone chips from the tibial shaft (normal bone) were placed in the cyst, and the wound was closed. A small pigmented area of skin from the right thigh was also excised for biopsy. Convalescence was uneventful. The patient was allowed to leave the hospital on April 15, 1944, with instructions to continue the aluminum acetate therapy.

Histopathologic Report—Capt Hans G. Schlumberger, M.C.
 "1 *Cuttings from bone cyst* Section consists of fusiform connective tissue cells, occasionally arranged in bundles and whorls. About 10-12 multinucleate tumor giant cells are seen (Fig. 6) per low power field. These cells contain from 3 to 14 nuclei and have a vacuolated polychromatic cytoplasm. Foam cells are scattered abundantly throughout the section and also form isolated nests. They are very prominent in a frozen-section stained with scarlet r. (The significance of these cells is minimized by Lichtenstein and Jaffe.)
 2 *Periosteum* Dense, longitudinally arranged bundles of connective tissue and part cells. No inflammatory or neoplastic cell-infiltrates are present.
 3 *Section of skin* The epidermis shows moderate keratosis and acanthosis. In the basal layer are many "cells clumps" having a clear cytoplasm and intimately related to adjacent nevus cells, many of which have a position and structure suggestive of Meissner's corpuscles. Masses of nevus cells are present in the uppermost layers of the corium, none have infiltrated into the deeper layers (Fig. 7). There is no evidence of malignancy.
Pathologic Diagnoses 1 Fibrous dysplasia of bone (Jaffe) 2 Dermal-epidermal nevus"

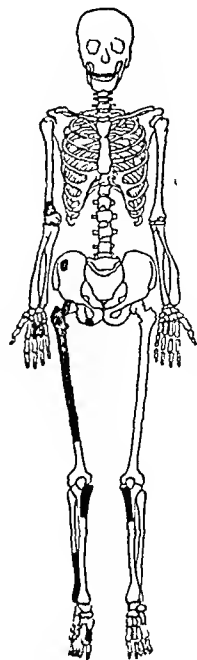


FIG. 5—Diagram illustrating areas of bone involvement. Note that they are predominantly unilateral.

COMMENT—Attention was first directed to this case by the occurrence of a pathologic fracture. This was true, also, in many of the reported cases. Fibrous dysplasia of bones is a prominent feature of Albright's syndrome, and is either unilateral or predominantly unilateral. There is no general decalcification of bones as is seen in hyperparathyroidism. The epiphysis often escapes involvement, though this was not true in our case. Early union of the epiphyses is part of the syndrome, so the patients are usually of short stature.

The pigmentation is typically patchy and unelevated. It has a tendency to follow nerve trunks in some of the reported cases. Although the etiology of the disease is not known, the unilaterality of the bone lesions and the tendency of the pigmentation to follow nerve distribution together with the endocrine disorder seen in the female patients suggested to Albright that the disease was one of central nervous system origin, possibly embryonal in nature.

The syndrome is more commonly seen in females than in males. The latter do not show the precocious puberty and early maturity of secondary sex characteristics, both of which were prominent features of our case. While no

determination of sex hormones was carried out in this case, such studies in other reported cases have uniformly failed to show abnormalities

Treatment—No specific form of therapy is known. When pathologic fractures occur, they are treated symptomatically and usually heal readily. In our case three fractures occurred in the same area of the same bone (right femur) and all healed at least as promptly as might be expected in uncomplicated fractures.

In addition, we unroofed two of the larger bone cysts, curetted the cavities and inserted bone chips. In the case of the femoral cyst this treatment seemed to arrest the extension of the cystic involvement. In the tibial cyst sufficient time

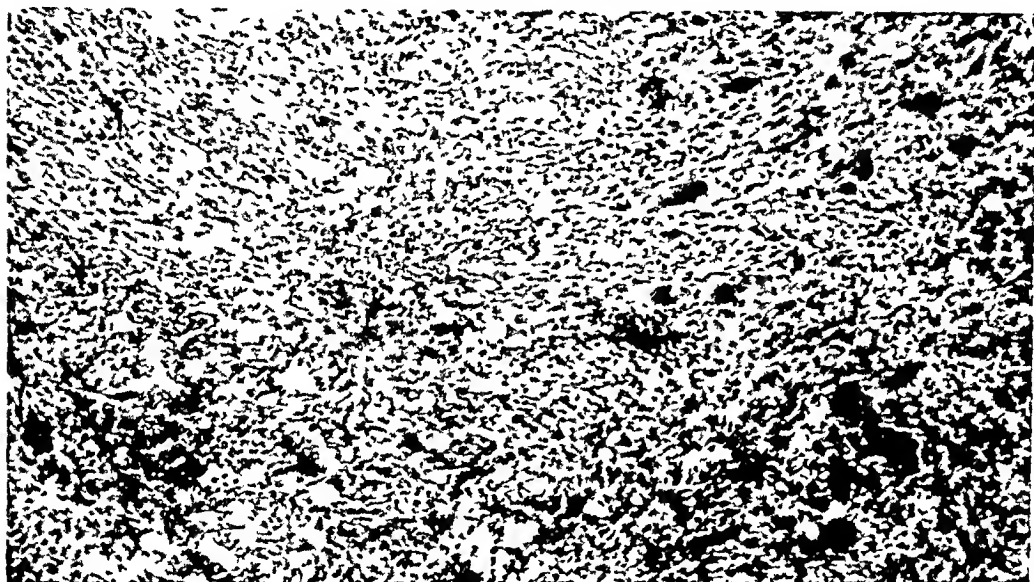


FIG 6—Curetings from bone cyst. Note the multinucleate tumor giant cells and fusiform cells ($\times 120$)
U S Army Medical Museum, Neg No 79195, Acc No 107988

has not elapsed to evaluate the result. We feel that operative interference is justified to obtain tissue for pathologic study for diagnosis. Insertion of bone chips appears to be of local therapeutic value.

We have also employed aluminum acetate therapy, as was done in the case reported by Dockerty, Meyerdig and Wallace³. The drug is given in the form of Burow's solution according to the formula suggested by Ghormley⁴ as follows: Sol aluminum acetate, 150 cc, Syr tolu, 90 cc, Honey q s ad 480 cc, Sig 4 cc q i d, p c.

It is recommended that at least one pint of milk a day be taken during treatment.

The use of aluminum acetate in the treatment of generalized fibrocystic disease of bone was suggested by Helfet⁵ in 1940. The treatment is based on a concept of calcium and phosphorus metabolism, which is at variance with generally accepted ideas. Helfet postulates that parathormone controls the blood inorganic phosphate level primarily and that variations in this level secondarily affect the mobilization of calcium. Aluminum acetate provides

ions which combine readily with phosphorus for excretion and serves to hoard calcium ions. Insufficient time has elapsed to ascertain the efficacy of this form of treatment. We can state that it has not been harmful even in doses of one dram of the prescription q i d. While additional cystic areas have appeared in the bones, the cysts already present have not enlarged during the period of treatment with aluminum acetate and there has as yet, been no regression of those already established.



FIG 7—Section of skin. Section taken through pigmented nevus. There is no evidence of malignancy (x 120). U S Army Medical Museum. Neg No 79194. Acc No 107988.

Several reported cases of Albright's syndrome have been subjected to exploration of the parathyroid glands; despite the fact that decalcification of bones is not generalized, there is no laboratory evidence of hypercalcemia, and no tumors of the parathyroid are found at operation. Such operations can serve no useful purpose in this condition and should be avoided. Since the manifestations of the syndrome are so striking, the indications and contraindications for various forms of therapy are definite, and so little is known of the true nature of the disease we feel justified in calling attention to this additional case.

SUMMARY

An additional case of Albright's syndrome is presented. The syndrome is characterized by fibrous dysplasia of bones, with cutaneous pigmentation.

in both sexes and gonadal dysfunction in females. Attention was first directed to this case by the appearance of a pathologic fracture in the right femur at the age of seven years. Two additional fractures occurred in the same area of bone in two years, and all healed well. Menstruation occurred at the age of three years for a three-day period, and the phenomenon was repeated similarly at the age of seven and eight years. Pigmentation of the skin was found to be scattered in the form of multiple small nevi, which followed no orderly distribution. Two enlarging bone cysts were unroofed, curetted, biopsies taken, and bone chips inserted. The material removed for biopsy had the gross appearance of decalcified bone spicules in the femur, and was soft, degenerated and waxy in the tibia. Response to aluminum acetate therapy has been inconclusive, but warrants further trial. Exploratory operation for removal of parathyroid glands is contraindicated. The etiology of the condition is a matter for conjecture, the treatment is empiric, and the prognosis uncertain.

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BRIEF COMMUNICATION

A SPLINT FOR INTRAVENOUS INFUSION

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THE STRAIGHT SPLINT which is generally used to immobilize the arm in the administration of intravenous infusions has been a part of our armamentarium until recently. We followed the usual procedure of immobilizing the arm on a straight board, well padded with gauze and cotton. The board was the length of the forearm and half way up the arm. The arm was stretched and tied to it with gauze. Both were then fastened to the bed. We had always been conscious of the fact that the arm during this procedure was not in the rest position, but did not know how to correct this. We felt that since the intravenous therapy was indicated and since that was the only way to give it, the patient's comfort had to be disregarded.

The immobilization of the arm with the straight splint inhibits body movements and the patient invariably complains of stiffness and cramping of the flexor muscles which progressively increases as the infusion proceeds. After the splint is removed the muscle fatigue at the elbow continues for several more hours. We thought that if the arm were in the position of slight flexion instead of full extension the patient's comfort would be increased and the complaints greatly diminished. In order to produce this degree of flexion we at first padded the protruding end of the straight splint, thus raising the forearm and producing flexion of the elbow. This method was not satisfactory because by anchoring the splint to the bed the arm lay in extension with the eventual discomfort to the patient. Of course placing the arm on a pillow would eliminate the full extension, but it would also prevent immobilization, resulting in needle displacement, with subcutaneous infiltration.

In view of the objectionable features of the straight splint it was generally felt for a long time that some modification was indicated, but the most marked incentive for the modification was the fact that one of the senior members of our staff had to receive an intravenous infusion. His discomfort, expressed in unequivocal terms, resulted in search for an improved splint. The three-angle splint which consists of three boards—a base which measures 24 inches in length, $5\frac{1}{4}$ inches in width and $\frac{1}{3}$ inch in thickness, an arm rest $16\frac{1}{4}$ inches in length, $4\frac{1}{4}$ inches in width and $\frac{1}{3}$ inch in thickness, an upright $6\frac{5}{8}$ inches in length, $5\frac{1}{4}$ inches in width, $\frac{1}{3}$ inch in thickness, and an arm extension which is a part of the base measures $8\frac{3}{4}$ inches. The upright is $5\frac{1}{4}$ inches at the base, tapering down to $4\frac{1}{4}$ inches at the upper end. The angle of the arm rest is approximately 45° . The tongues of the upright

at each end fit into the consecutive grooves of the arm rest and the base. The arm rest is attached to the arm extension by means of a dowel. The edge of the arm extension is tapered off to relieve the pressure of the splint on the upper arm. The wide base prevents tilting of the splint. The arm extension and the arm rest are covered with a mattress of leatherette, the mattress is fastened to the splint at three points, at the apex of the arm rest, at the angle, and at the end of the arm extension. Two sets of leather straps

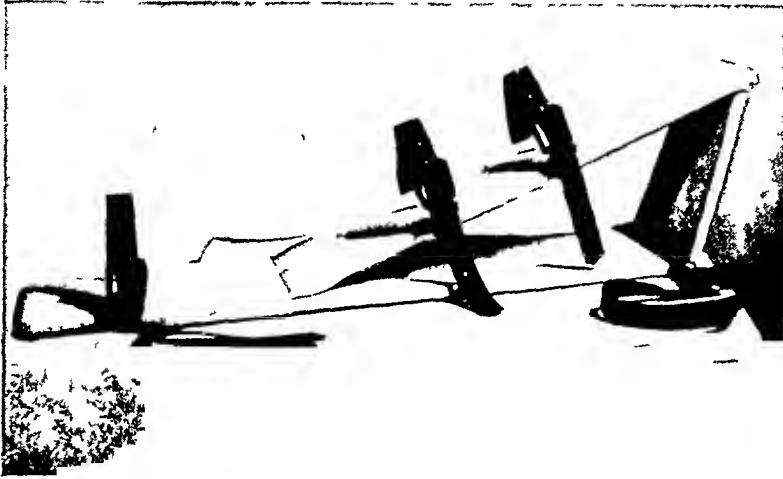


FIG 1—Mattress padded splint for intravenous infusions



FIG 2—Lateral aspect of the splint in actual use, showing the angulation and immobilization of the arm

with buckles are attached to the arm rest, one set to the arm extension, to immobilize the arm and the forearm. One pair is also placed at the base near the upright to fasten it to the bed.

A three-angled splint which is covered with a mattress and leather straps is ready for intravenous infusion at a moment's notice. This is not the case with the commonly used straight splint. There is much lost motion in its preparation. The nurse or doctor has to prepare the splint by padding it with cotton and wrapping it with bandage. This preparatory procedure consumes much valuable time which is actually wasted, since the padding can be

used for the one patient only and must be discarded before repadding the splint for the use of the next patient. Then the nurse spends time in bandaging the arm to the splint and the splint to the bed. The loss of time and the wasting of material is completely eliminated with the use of our splint, since its application is instantaneous.

In patients with small, deep-seated veins it may be more advantageous to introduce the needle before immobilizing the arm. Of course if a vein in the forearm, wrist, or back of hand is used this splint offers added advantages.

The length, the width and the thickness of the splint do not necessarily have to be measured to the tenth of an inch—we are simply stating the exact measurements of our splint. The length of the arm rest and arm extension may be about 26 inches, so that the greatest part of the arm and forearm in the adult come to rest upon it. To accommodate the younger patients the base board would have to be proportionately less in length. The upright should be six to seven inches in order to form about a 45° angle. The dowel, tongue and groove are only a mechanical finesse. Ordinarily, simple nailing of the parts will suffice. The mattress and leather straps were added to eliminate the repeated use of cotton and gauze, as a time-saving device, and also as a sanitary precaution. The mattress may be covered with oilcloth, thick cellophane, or any other waterproof material which can easily be cleansed of blood and other fluids.

If a mattress is not desired, the planed and waxed wooden angular splint when covered with one layer of gauze provides sufficient padding for the resting arm. The advantages of this splint as we have found it in actual use are as follows:

- (1) It is ready for instantaneous use.
- (2) The cramping and stiffness of muscles are reduced to a minimum—much appreciated by the patients.
- (3) It takes the weight off the forearm, thus reducing the muscle fatigue after removal of the splint.
- (4) Patient has more freedom of action and can turn from side to side.
- (5) It is easier to fasten the arm to the splint and the splint to the bed for complete immobilization.
- (6) The leather straps immobilize the arm and the forearm, thus eliminating the constant addition of gauze in a given case.
- (7) The mattress eliminates the repeated padding with cotton and gauze with each successive infusion. It is a time-saving device.
- (8) In our hands we found that the use of this splint tends to make an intravenous infusion an exact, clean, comfortable, economical and time-saving procedure.

BOOK REVIEW

HYPERTENSION AND HYPERTENSIVE DISEASE By William Goldring, M D, and Herbert Chasis, M D New York, The Commonwealth Fund (1944)

Doctors Goldring and Chasis' book is a brief but thorough discourse on a subject around which an enormous literature has grown. In clear, concise and simple language the authors encompass the field of hypertension and related nephritis from their point of view. It is their thesis that hypertension presents a so-called malignant phase only because of nephrosclerosis. Accordingly, the clinical term "malignant hypertension" is mentioned. The surgical aspects of hypertension, including the operations of sympathectomy and splanchnicectomy, are treated briefly. On the other hand, there are great details in the appendices for a student of the subject in its nonsurgical aspects. The book provides an excellent approach to the subject for the student and the physician.

HAROLD NEUHOF, M D

EDITORIAL ADDRESS

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REPORT ON IMMERSION FOOT CASUALTIES FROM THE BATTLE OF ATTU

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NEW YORK, N Y

FROM THE SURGICAL BRANCH MCCAW GENERAL HOSPITAL, WALLA WALLA, WASHINGTON

TWO GROUPS OF PATIENTS with immersion foot have been observed and treated at McCaw General Hospital since June, 1943. The first group consisted of 25 patients who were admitted to the hospital with varying degrees of sepsis and gangrene of the feet, arriving approximately three weeks after having been removed from combat duty on the island of Attu. The second group of patients, numbering 27, consisted of cases admitted here at intervals by transfer from the Northwest Pacific area, with subjective complaints of delayed or latent disturbances of the feet coming on approximately six months or more after exposure during the battle of Attu.

GROUP I

The original group of 25 patients admitted shortly after combat duty on the island of Attu will be discussed first. Nine of these patients were evacuated from the scene of action primarily because of battle wounds (gunshot, shrapnel, *etc*), the remainder were evacuated because of their immersion foot condition. These soldiers averaged about 21 years of age, had had previous intensive training in the maneuvers of just such battle conditions as island landings and invasions, similar to conditions which they encountered in Attu, and they had been presumably selected for this invasion assignment because of their excellent physical condition, qualities of endurance and temperament. They all traveled to the Aleutians from California by submarine or transport, stopping over *en route* for one day at Dutch Harbor.

The men all wore two pairs of socks (one pair woolen) and carried an extra pair in their packs. They were equipped with leather boots which reached to about four inches below the knee, a few of the boots had rubber soles. A group of ten men who came up on submarine were unable to change their socks or shoes for about four days before going into battle because of cramped conditions on the submarine and the constant alert status. Because of battle conditions, they were unable to change socks or shoes during the action on the island, and, therefore, these men average about ten days

Fig 1



Fig 1—Amputation—Revision through proximal third of metatarsal region, with coverage of skin defect of plantar surface by pedicle flap from right thigh *
Fig 2—Right Revision—Amputation through proximal phalanx right first toe
Fig 3—Right Foot Revision of portion of distal phalanx first toe
Left Foot Amputation—Revision just proximal to head of first metatarsal, and through proximal phalanges, second third, fourth and fifth toes
* The numerals on the photographs do not denote their sequence, but represent a marking for military record

IMMERSION FOOT CASUALTIES

without a change of socks or shoes. These ten men were the most severe cases of gangrenous immersion feet. The other 15 men came up on transports and were able to change socks or shoes up to the time of battle. They averaged three to six days without change of socks or shoes during their action on the island, they were the milder cases.

FIG 4A

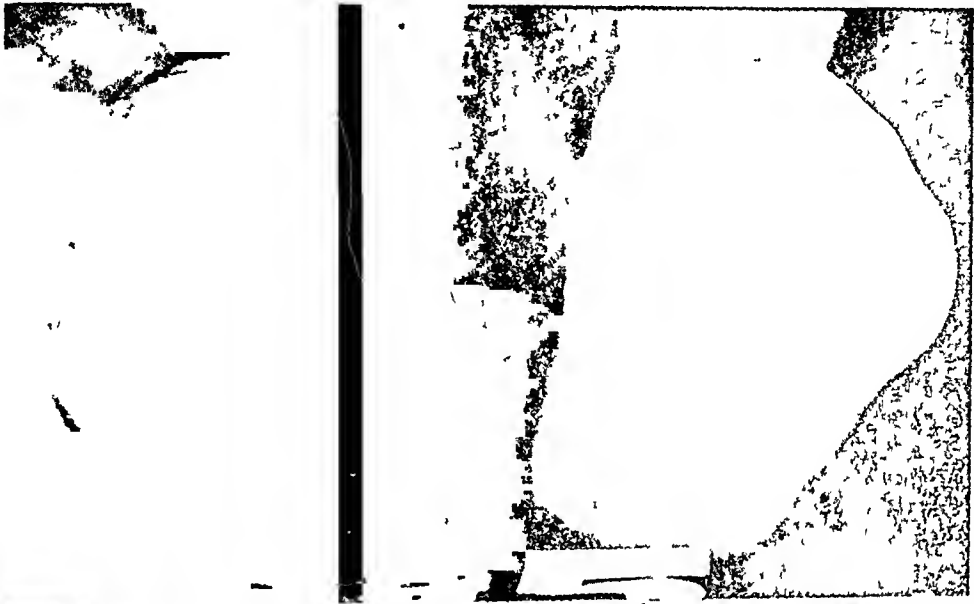


FIG 4B

FIG 4—Revision—Amputation proximal to metatarsal heads, both feet

These 25 men were among the advance Scouts of the invasion and went from submarine and transport to the island by means of rubber boats. Their feet and legs became wet almost immediately on landing. They had been instructed to discard all their equipment on contacting the enemy (6 to 12 hours after landing on the Island). They were, therefore, all practically

without food throughout their stay in action, an average of about six days, and they had discarded their extra boots and socks, as well as other equipment. From what can be ascertained, the temperature ranged around 35° F, and there was practically a constant damp fog. The men were forced to lie in ravines, gullies and foxholes for long periods of time in cramped, inactive positions, their feet and legs usually immersed in cold water because of the melting snows. Except for an occasional hour or



FIG 5—Right Foot Revision—Amputation at metatarsal heads (first, second, third, fourth) and proximal phalanx fifth toe
Left Foot Proximal to head first metatarsal, at heads second, third metatarsals, proximal phalanges fourth, fifth toes

two, the men received no real physical rest or sleep during their stay in action.

Aside from general fatigue, exhaustion, numbness and discomfort of the feet, these soldiers had relatively little actual pain in the feet or legs until the shoes were removed when they were taken out of action. Of the men with battle wounds, three men had lost large amounts of blood. Almost immediately after removal of shoes and socks in all cases there was an onset of extreme swelling and pain in the feet, and in 6 to 12 hours there occurred blackish discoloration of variable portions of the feet. Gangrene, first dry, then septic, set in. The men were removed to hospital ships as rapidly as possible (from 4 to 24 hours). Immediate treatment consisted of plasma in some cases, generalized application of warmth, warm food and drink and morphine for control of pain. Local treatment of the feet consisted of repeated sprays with some sulfanilamide spray preparation followed by the application of sterile dressings. All cases received sulfanilamide by mouth.

The men were evacuated from Attu by ship to Barnes General Hospital as rapidly as conditions permitted, after a stay of about four days at Barnes General Hospital, they were transferred to McCaw General Hospital. Almost all of the cases were running a low grade temperature with the exception of the most severe cases who ran septic elevations of temperatures. The men all appeared physically exhausted. Almost all the men had blood counts showing lowered red count, lowered hemoglobin and moderate to high leukocytosis. Six patients were given one or more blood transfusions shortly after admission here. All patients were placed on non

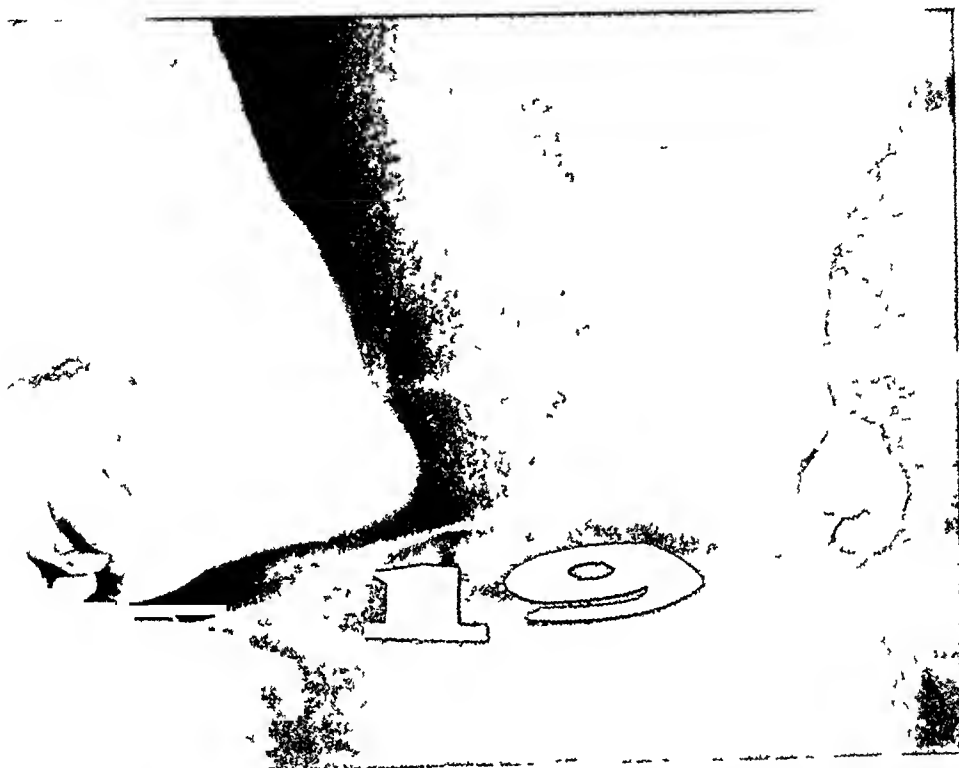


FIG 6—Right Foot *Revision*—Amputation proximal to head first, second metatarsals. Left Foot *Revision*—Amputation at head of first metatarsal and through proximal phalanx of second toe. Note Severe flexion contractures of other toes, subsequent amputation—revisions performed through old remaining proximal phalanges.

high vitamin concentrate therapy and high calorie diet. Ten feet of the 25 cases showed little or no evidence of gross tissue loss. Ten feet had desquamation or separation of blackish superficial tissue without need for further surgical procedures. Thirty feet required immediate débridement of gangrenous, suppurating soft and bony structures of both feet of variable degrees. Severity of gangrene involved the great toes most often, other toes next in frequency, and the remainder of the feet next. The wounds were left wide open for drainage, and skin retraction was prevented by application of liquid adhesive and stockinette traction. Following débridement, local therapy of the feet consisted of dressings of Azochloramid in triacetin, activated zinc peroxide emulsion, or normal saline dressings as the individual case required. Wherever possible, the intact skin in the region of the wounds was covered with a protective coating of compound tincture of benzoin on which was applied a mixture of zinc oxide ointment and castor oil to prevent

FIG 8A



FIG 8B



FIG 8C



FIG 8A—Revision—Amputation through proximal third of metatarsal region of right foot
FIG 8B—Plaster molds of feet used to make prostheses worn inside shoe
FIG 8C—Latex rubber molds attached to foot supports after amputation—revision through distal third of metatarsal region, both feet

IMMERSION FOOT CASUALTIES

irritation from the drainage material and antiseptic agents. Large, massive loose dressings were applied to insure protection from pressure and to maintain intrinsic warmth. In all cases the peripheral arterial pulses were of excellent quality. There was little or no evidence of elevation ischemia, but there was considerable bluish mottling of the skin of the feet on dependency. Only two cases presented marked evidence of peripheral vasomotor disturbances (palpable coldness, clamminess, hyperesthesia) on examination at time of admission. In almost all cases, tissue damage or destruction was considerably greater on the left foot than on the right. There was no apparent explanation for this finding.

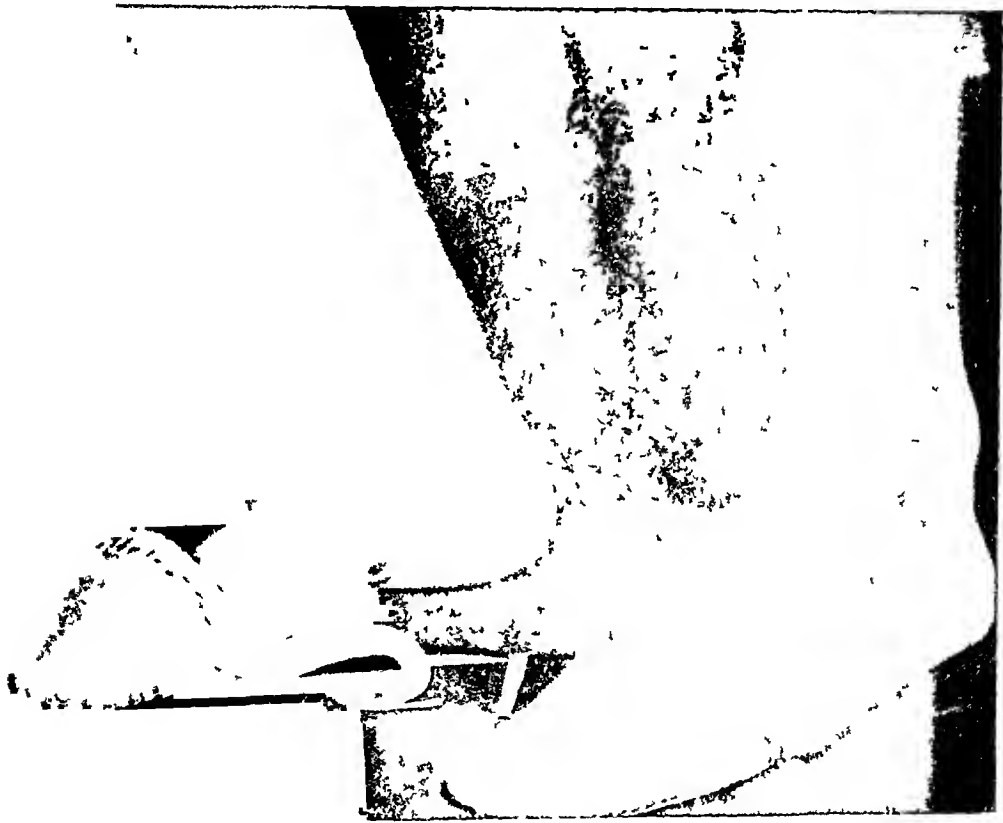


FIG 7—Latex rubber molds used to fill space in distal portion of shoes, after amputation revision through distal metatarsal region of both feet

Following initial surgical débridement, the 30 feet required one or more subsequent surgical procedures for plastic revision and closure of the wounds of the feet, in all, a total of 64 operative procedures. Six feet required amputation and revision of the first (great) toes alone, just proximal or distal to the first metatarsophalangeal joint, as local conditions of the tissues permitted. Eight feet required minor partial amputations of the second, third, fourth, and fifth toes in some cases in addition to amputation of the great toes. Six feet required amputation and revision through the distal metatarsal regions. Three feet had amputation and revision through the proximal third of the metatarsal regions. One foot had a transmetatarsal disarticulation. In all cases of amputation and closure through the metatarsal regions skin closure was facilitated by undercutting and advancement of the

full-skin thickness. One case, after débridement through the metatarsal region of the foot and loss of about two-thirds of the skin on the remaining plantar surface of the foot, required a pedicle flap from the opposite thigh to obtain a full-thickness skin covering. This was done as a two-stage procedure, and an excellent soft, thick, flap covering was obtained. Four split-thickness skin grafts were performed for covering of defects on dorsum of feet. Two operative procedures for straightening of rigid flexed toes were done. In one case revision of all the distal phalanges was done for rigid flexion deformities.



FIG. 9.—Right Foot Revision—Amputation through proximal phalanx first toe.
Left Foot Revision—Amputation proximal to first metatarsal head, through proximal phalanges second, third, fourth, and fifth toes.

All of the feet healed completely and the patients are walking without any difficulty. All of the patients were sent home on a convalescent furlough, and on return were observed for any development of pressure points on the feet, where pressure points were noted, correction was made by proper modification of the shoes. As soon as patients were healed and ready to walk they were supplied with low quarter shoes and made-to-measure arch supports. In some cases plastic rubber prostheses were made to fill up space defects in the shoes and to prevent the foot from slipping forward on walking. In those cases in which there was loss of a considerable portion of the foot, plaster molds were made to permit accurate construction of prostheses. On resumption of walking these patients have had surprisingly little or no discomfort from wound scars and there has been little edema or other evidence of impaired peripheral circulation (with the exception of two cases previously noted).

Throughout hospital treatment vascular exercises of the lower extremities

IMMERSION FOOT CASUALTIES

were conducted three times a day in an organized class fashion under the direction and supervision of one of the soldiers. As soon as the local condition of the extremities and wounds permitted, patients received physiotherapy in the form of whirlpool, massage or muscle stimulation as the individual case required.

All of the original group of 25 patients were walking well, without need for crutches, cane or any other type of support at the time of discharge from the hospital. Those patients who suffered loss of distal portions of the feet involving all or any part of the metatarsals were able to walk surprisingly well when, in addition to fitted arch supports, a spring steel

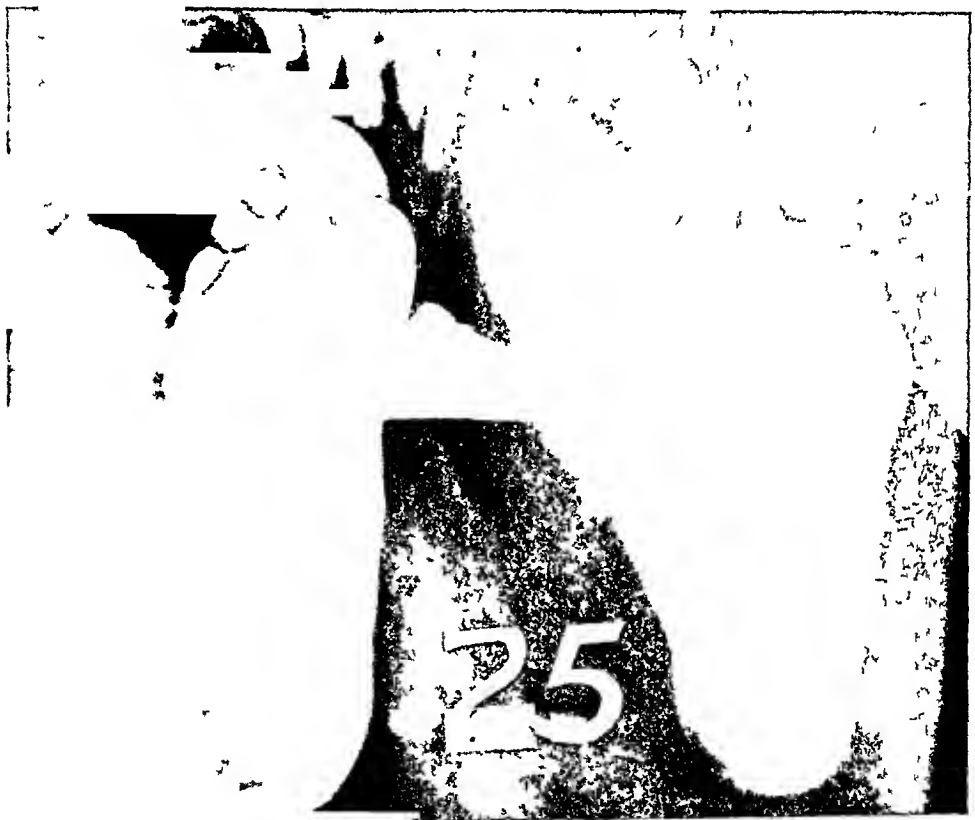


FIG 10—After surgical correction of deformity of both second toes

longitudinal strip was incorporated in the sole of the shoe. In some cases a transverse leather bar was added to the sole of the shoe, back of the metatarsal heads, in place of the transverse arch support usually placed inside the shoe. This modification seemed to supply a fairly satisfactory substitute for the "spring" of the metatarsophalangeal joints which is probably necessary in the take-off of each step. In those feet in which tarsometatarsal disarticulation was performed, there was no evidence of distorted tendon pull and there was normal stable body weight-bearing on the remnant of the foot.

It was noted that soon after getting up and around, many of these patients developed evidence of a dermatitis of the feet, probably a manifestation of dermatophytosis. This condition responded promptly to treatment with potassium permanganate foot soaks, application of a boric-salicylic acid

foot powder to the feet and socks and shoes, and rigid enforcement of proper hygiene of feet, socks and shoes for all the men on the ward

Two lumbar sympathectomies were performed for those feet showing evidence of severe vasomotor disturbances, sympathectomy was performed prior to final plastic revision and closure of the feet. Surgical healing and

FIG 11A

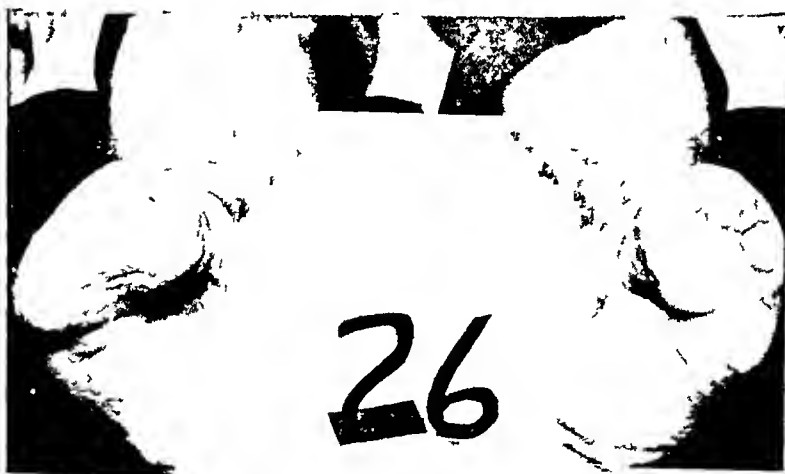
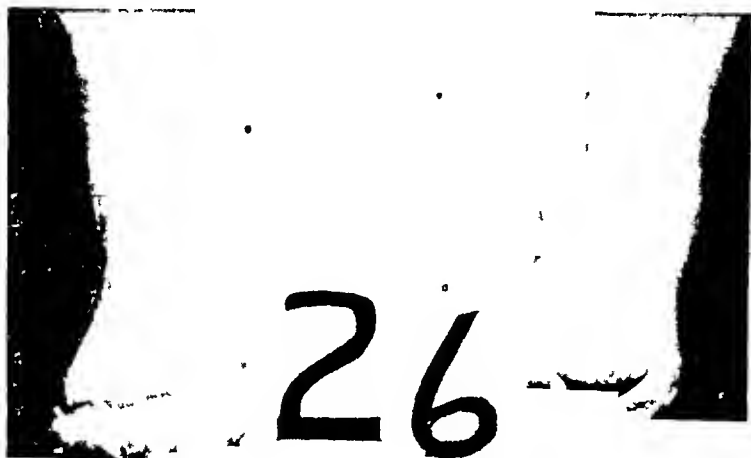


FIG 11B

FIG 11A—Right Foot Revision—Amputation through proximal third metatarsal region
B Left Foot Revision—Amputation at tarsometatarsal joint, medial plantar surface covered by pedicle flap skin graft

relief from coldness, clamminess and hyperesthesia has been good. Of the original group of 25 patients, two patients have returned to duty. The remaining patients have been separated from the service because of their inability to continue infantry duty and their lack of any other training or qualification which could be utilized in any other capacity.

MICROSCOPIC PATHOLOGY

All tissues removed at operations were carefully studied microscopically by Major Lawrence C. Milstead, Chief of Laboratory Branch, and several interesting findings characterized these tissues. The most prominent feature

was a marked generalized fibrosis and collagen deposition. Numerous small blood vessels and nerves were seen embedded in this dense fibrous and collagenous material. The surface epithelium in most sections showed a tendency to hyperkeratosis. There was evidence of extensive proliferation of the endothelial layers of almost all blood vessels with evidence of attempted recanalization of the lumen. The smaller arteries and veins showed almost complete obliteration of the lumen and some of the larger vessels showed obstruction of the lumen by dense connective tissue. There was also evidence



FIG 12—Right Foot. *Revision*—Amputation through proximal third of first metatarsal, just proximal to heads of second, third, and fourth metatarsals, with removal of fifth metatarsal.

Left Foot. Through mid first metatarsal, and through distal third of second, third, fourth, and fifth metatarsals.

of inflammatory round cell and plasma cell infiltration in the perivascular spaces.

GROUP II

The second group of patients, numbering 27, consisted of cases admitted here at intervals by transfer from the Northwest Pacific area with subjective complaints of delayed or latent disturbances of the feet coming on approximately six months or more after exposure during the battle of Attu. These patients came into battle somewhat later than Group I and were subjected to somewhat less severe environmental and battle conditions than those of the group who suffered severe tissue loss of the feet and who were admitted to McCaw General Hospital shortly after the battle. The majority of these patients complained of aching, burning pain in the toes and varying degrees of sweating and cold clamminess of the feet. However, increased local warmth, as well as cold, caused an aggravation of discomfort. Lumbar sympathetic blocks were performed in all cases with maximum temperature response in all, but with variable degrees of subjective relief of discomfort during block. In 15 of these cases the physical findings and discomfort were

minimal and these patients have been returned to some form of limited duty in temperate climates not requiring excessive standing or walking. In ten cases there were physical findings of moderate to severe vasomotor disturbances characterized by coldness, excessive sweating of the feet, and aching in the toes. In three cases there was evidence of moderate stiffness and rigidity of the toes, in addition to moderately severe vasomotor findings. In these three cases, study by lumbar sympathetic block indicated marked clinical relief of symptoms during block and surgical lumbar sympathectomies were subsequently performed in these cases. The seven other cases are still being observed at the present time.

The patients who have received lumbar sympathectomy have been observed postoperatively for four months at this writing. Although they are considerably more comfortable as the result of warm, dry feet, with increasing physical activity they are beginning to notice a partial return of the subjective complaint of aching of the toes. Observation over a long period of time will be necessary to properly evaluate the efficacy of lumbar sympathectomy in these and other postimmersion feet with subjective residual symptoms of a vasomotor character.

The gradual development of clawtoe deformities of the feet in some of these cases has been a troublesome complication. The condition can probably be explained on the basis of the exaggerated deposition of collagenous and fibroblastic material in the tissues following immersion foot exposure with subsequent gradual contractures. In some cases there was definite evidence of a tendency to a congenital clawing of the toes, with aggravation by the immersion foot exposure. Where rigid contracture of the toes occurred, with friction-irritation from the dorsal aspect of the shoe, surgical procedures for straightening of the toes were performed. The performance of repeated lumbar sympathetic block, or surgical lumbar sympathectomy, had no apparent effect on the development or progress of the clawtoe deformities.

The persistence of pain in the toes and feet is probably related to the extensive perineural fibrosis, as demonstrated in tissue sections. With late, progressive contracture of this perineural fibrosis, the delayed aggravation of pain in some cases may be explained.

COMMENTS

1 The provocative factors involved in the causation of these cases of immersion feet are fairly well understood, and have been encountered in many other military campaigns. The most important of these factors are (a) Increased susceptibility to lowered environmental temperature (but above freezing) as a result of increased conductivity of the constantly wet skin, (b) vascular stasis of the extremities as a result of prolonged periods of inactivity while lying in foxholes, ravines, *etc*, (c) The effects of hypoproteinemia and vitamin depletion (from lack of food) on capillary permeability, (d) the effects of loss of blood in those patients who were wounded.

FIG 14



FIG 13



FIG 16

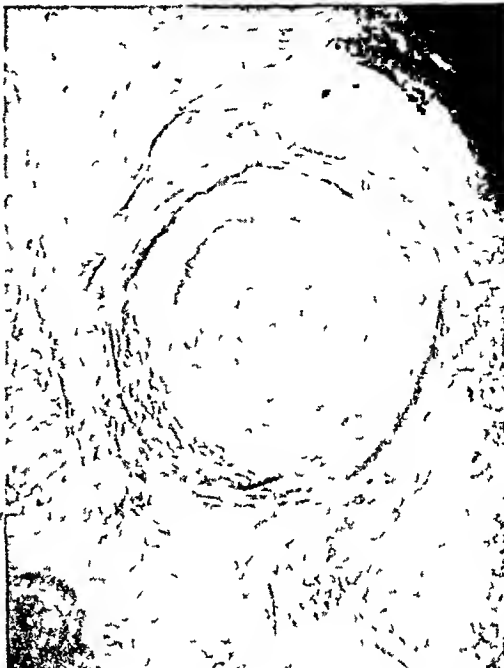


FIG 15



FIG 13 — Obstructed artery, subcutaneous tissue, showing endothelial hyperplasia and recanalization (x 64)

FIG 14 — Arteritis Organizing thrombus (x 64)

FIG 15 — Perineural fibrosis Deep tissues of sole of foot (x 64)

FIG 16 — Organized thrombus, perivascular fibrosis, subcutaneous tissue of great toe (x 24)

The prophylactic measures to be considered are self-evident, but must necessarily be governed by battle conditions

2 Most of the tissue injury presumably occurs during this so-called "thawing out" period, that is, when the wet shoes or boots were removed, there was a sudden flooding or choking of the tissues with fluid. Such "choking" of tissues of the extremities with fluid is probably related to extensive vasodilation, possibly as a result of the accumulation of a toxic histamine-like substance in the tissues, as well as the other provocative factors of the immersion period. Thrombosis of smaller-sized blood vessels is undoubtedly related to the sudden increase in pressure within the tissues of the extremities. The extent of tissue necrosis and gangrene is obviously dependent upon the extent and severity of the choking of the tissues and the thrombosis, and the degree of recanalization of end vessels of the extremities. The deposition of large amounts of fibrinogen-rich transudate, collagenous and fibrous material is eventually responsible for contractures, hardening, and pain in the soft tissues of the feet and toes.

The therapeutic implications are concerned with the prevention or control of the severe outpouring of fluids or transudate into the tissues of the extremities. The measures which suggest themselves are (a) elevation of the lower extremities, (b) *immediate application* (on removal of shoes or boots) of *pressure dressing support* to the extremities in the form of Ace bandages, gum rubber bandages, Unna's paste boots, or possibly a light plaster encasement, (c) the local application of *cold* to the extremities, (d) the intravenous administration of hypertonic agents (plasma, glucose, etc.) to control transudation, and (e) the possible improvement of vasoconstrictor tone by the use of adrenalin.

3 Careful observations indicate that amputation revisions through the feet, as far back as the tarsometatarsal joints, have provided satisfactory functional results for standing and adequate walking. In standing, the preservation of a stable tarsus sustains the mechanical arches of the feet, and the ligaments and muscles act to balance body weight on the tarsals. For walking, mobility at the metatarsophalangeal joints is necessary for the spring-like take-off of each step. The use of the spring-steel longitudinal strip in the sole of the shoe, and the transverse leather bar on the sole of the shoe placed back of the distal ends of the revised metatarsals, have materially improved walking. Insistence on continual care and hygiene of the feet has been stressed.

4 The status of late vasomotor disturbances in these immersion feet cases is still indefinite and difficult to evaluate. In Group I, the severe cases with gangrene and loss of portions of the feet, there were few signs and symptoms of latent vasomotor imbalance. In Group II, the presumably milder cases without any tissue loss, which were received at this hospital many months after their original immersion exposure, the incidence of findings of vasomotor imbalance was high. The reasons for this situation are not clear, and may be related to constitutional sympathetic nervous system instability.

of the individual patients. At any rate, therapeutic attempts by repeated lumbar sympathetic novocaine blocks in all the cases of Group II, and by

FIG 17

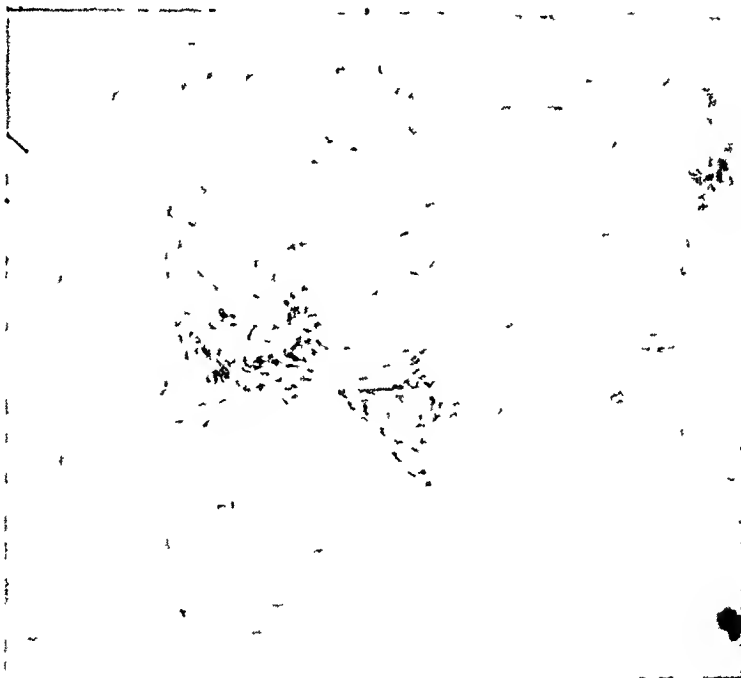
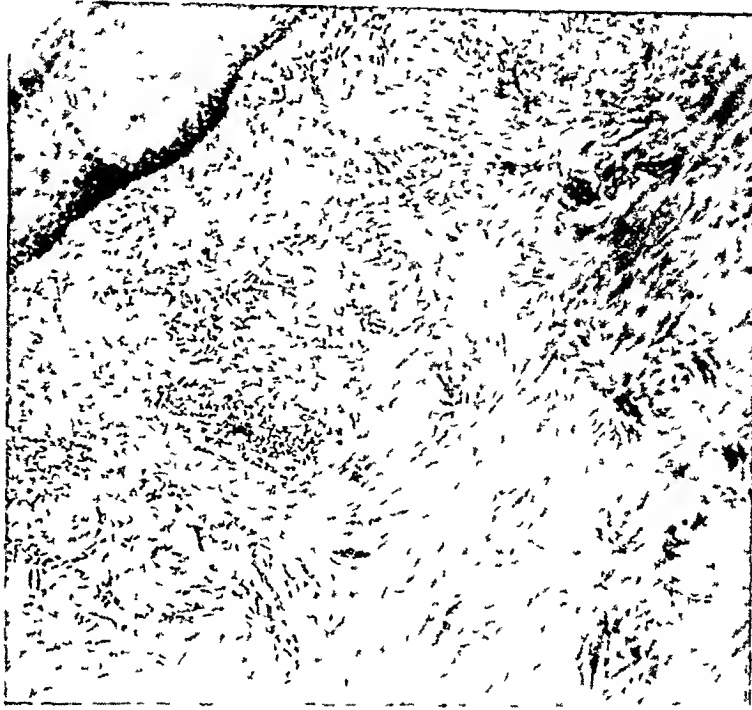


FIG 18

FIG 17—Inflammatory fibrosis of skin, foreign body giant cells present ($\times 64$)

FIG 18—Collagen replacement in subcutaneous tissue ($\times 80$)

surgical lumbar sympathectomy in a few cases, have yielded disappointing results

Valuable cooperation and guidance in the management of these cases was rendered by Captain William Scoville, Chief of Neurosurgical Section, Major George Waters, Chief of Orthopedic Section, and Lt Col O S Harbaugh and Lt. Col J D Lamon, Jr, of the Surgical Branch

TRANSTHORACIC RESECTION OF THE ESOPHAGUS AND STOMACH FOR CARCINOMA*

ANALYSIS OF THE POSTOPERATIVE COMPLICATIONS, CAUSES OF DEATH,
AND LATE RESULTS OF OPERATION

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THE TECHNICAL ADVANTAGES of the transthoracic approach are now well established in the surgical management of certain cases of carcinoma of the esophagus and of the cardia and fundus of the stomach. Starting with the cases of carcinoma involving the cardia and fundus of the stomach or the esophagus close to the cardia, the application of this procedure has been extended during the past three years to include many cases requiring a total gastrectomy and more recently, by effecting certain modifications of the technic of operation, resections with anastomosis have been performed high in the chest for the removal of midesophagus lesions.

In general, from the standpoint of the operative technic to be used, the cases can be arranged in three groups according to the location of the growth: (1) *Lesions in the middle half of the thoracic portion of the esophagus*. These require an esophagectomy with a high intrathoracic esophagogastric anastomosis, either just above or just below the aortic arch (Fig 1). (2) *Lesions arising in the lower esophagus or fundus of the stomach*. In this group the resection includes a portion of the esophagus and a relatively large segment of the upper half of the stomach. An esophagogastric anastomosis low in the chest is carried out (Fig 2). (3) *Lesions which involve the major portion of the stomach but which invade the cardia and often the lower esophagus*. These require a total gastrectomy followed by an esophagojejunostomy low in the chest (Fig 3).

The cases in Group 1 present a rather special problem which is dealt with in greater detail in another place¹. Those in Groups 2 and 3 belong together under the heading of transthoracic gastric surgery. With occasional modifications of minor importance the techniques described in two former communications were used in these cases^{2, 3}. Descriptions of the techniques of these several procedures will, therefore, be omitted here.

From 1939, when the first transthoracic gastric resection was performed at the Massachusetts General Hospital, until the present (November 1, 1944), 127 patients with carcinoma of the stomach or esophagus have been operated upon by the transthoracic approach. Chart 1 illustrates the grouping of these cases as to location and type of operation performed.

There were 85 cases of carcinoma of the stomach or lower esophagus invading the cardia. In 24 of these the disease was inoperable and no

* Read before the New York Surgical Society, December 13, 1944

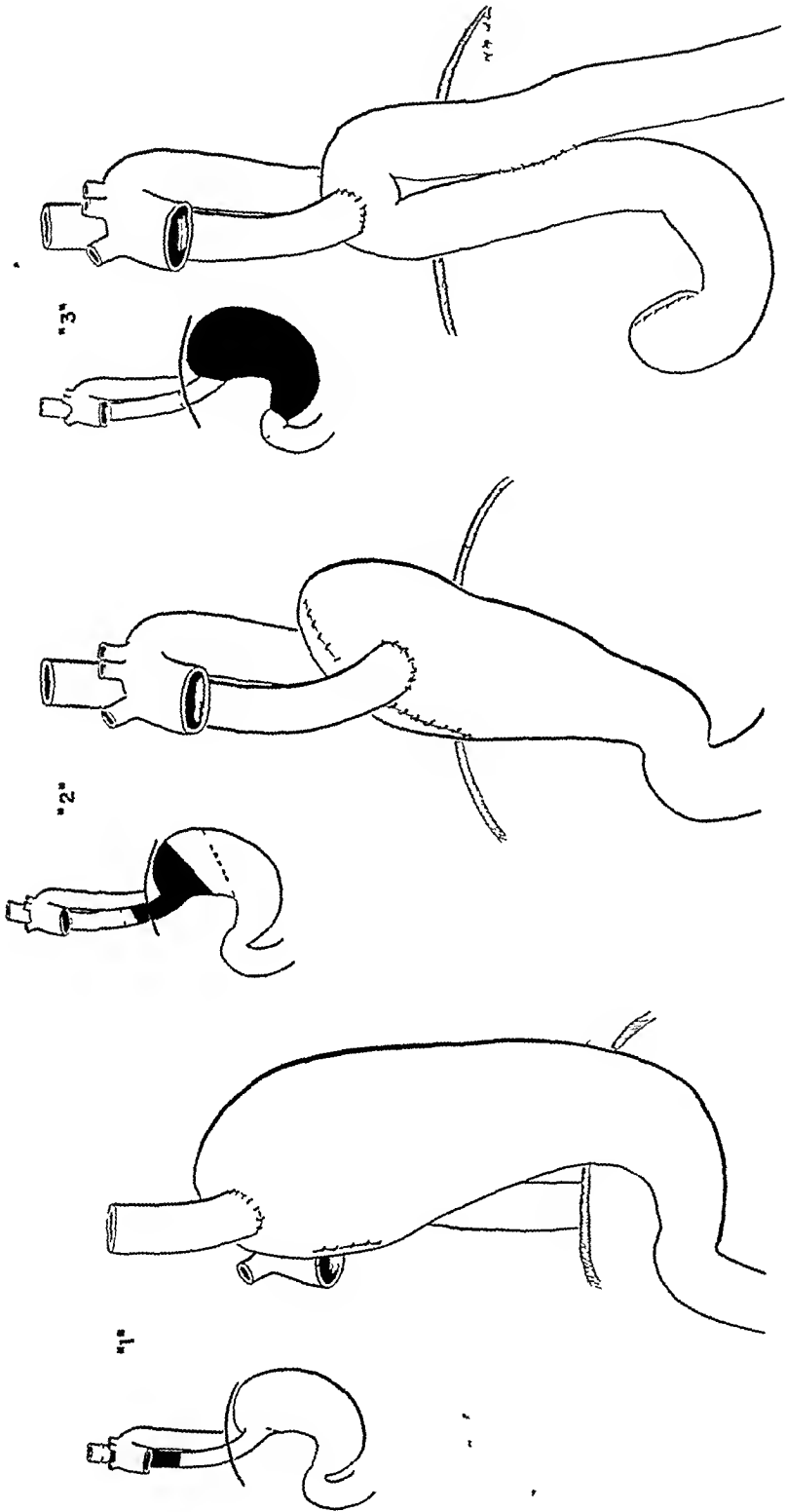


Fig 1

Fig 2

Fig 3

Fig 1.—Diagram illustrating arrangement of viscera after completion of operation for resection of carcinoma of the midthoracic portion of the esophagus. Stomach drawn high in the chest, esophagus divided above the aortic arch, and anastomosis placed in front of arch. Insert shows the region in the esophagus where the tumor lies in these cases.

Fig 2.—Diagram illustrating arrangement of viscera after resection of lower esophagus, cardia, and fundus of stomach. Distal segment of stomach drawn into chest 10" a low intrathoracic esophagogastric anastomosis. Insert shows the region involved in this type of case.

Fig 3.—Diagram illustrating arrangement of viscera after total gastrectomy with intrathoracic esophagojejunostomy. Insert shows region involved in such cases (entire stomach).

resection was carried out. A resection and anastomosis was carried out in 61 cases. This makes a resectability in the gastric and lower esophagus cases of 71.7 per cent (of cases operated upon). Of the 61 cases of resection, ten lesions were low in the esophagus and 33 were in the fundus or cardia of the stomach, making 43 cases of partial resection of the stomach and esophagus followed by an esophagogastric anastomosis low in the chest. In the remaining 18 cases so much of the stomach was involved that a total gastrectomy was required. In these an esophagojejunal anastomosis was performed.

The middle esophageal carcinoma group included 42 cases. Of these, 17 were found to be inoperable. In 25 cases a resection was carried out, but in only 11 of these was a high intrathoracic esophagogastric anastomosis performed. This operation has been in use in this clinic only during the past year (1944). Previous to that the Torek operation was used. The latter was performed in 14 cases. These will not be discussed in this paper, in which it is intended to deal only with the cases in which an anastomosis was performed. The resectability for the entire group of 42 midesophagus cases was 59.5 per cent.

Age of Patients Operated Upon—Before discussing the complications and causes of death following resection, it is important to realize that a relatively large proportion of the patients subjected to operation were of advanced age. Table I gives the number of patients in each decade.

IMMEDIATE RESULTS OF OPERATION

(A) *Inoperable Cases Explored*—Exploration by the transthoracic route is a relatively benign procedure if one takes into account the nature of the disease and the almost universally poor condition and advanced age of the patients operated upon.

Cases were considered to be inoperable when metastases were found in the lung, the liver, or in the peritoneum, or when the primary tumor was too adherent or was invading adjacent tissues or organs excepting the spleen or tail of the pancreas which could be removed. Regional lymph nodes containing metastases were removed in resectable cases along with the growth. In several cases a resection was performed even when involved nodes which were inaccessible had been found. The removal of an obstructing growth in such circumstances was considered to be justifiable because of the palliative relief which was brought about by the operation. In general, a radical approach to the problem was adopted and any growth which could be resected was removed, always hoping to effect a cure but actually expecting in the majority of cases a reasonable degree of palliation.

Of the 17 patients with inoperable carcinoma of the midthoracic esophagus who were explored through the chest, four died in the hospital. The causes of death were in one case perforation of the aorta by direct extension of the tumor, in two cases mediastinitis from perforation of the growth, and in another case aspiration pneumonia. Of the 24 patients with carcinoma of

RESECTION OF ESOPHAGUS AND STOMACH

SPECIAL PROCEDURES ADOPTED IN TREATMENT OF 127 PATIENTS WITH CARCINOMA
OF THE STOMACH OR ESOPHAGUS

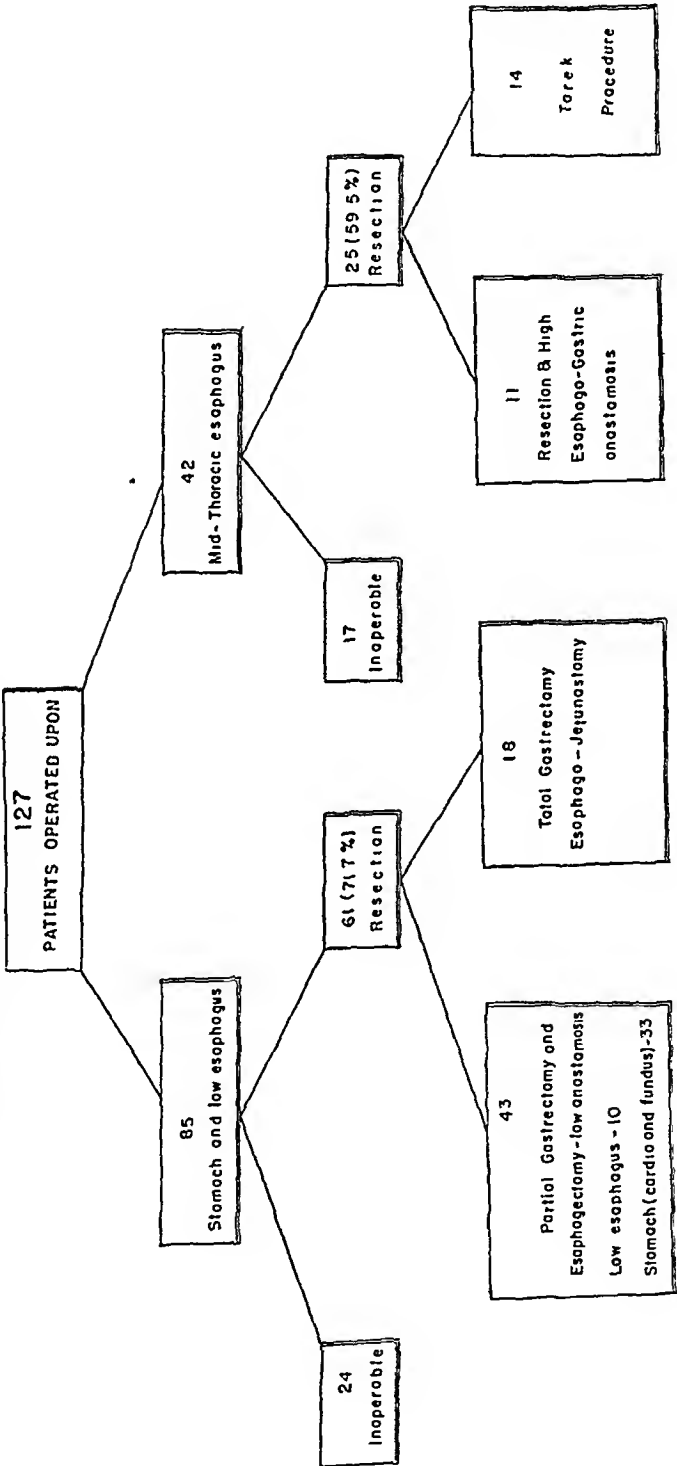


CHART I

the stomach and cardia who were found to have an inoperable tumor, two died of pneumonia and one of an undetermined cause. There were, therefore, in all, seven postoperative deaths in the total group of 41 patients who were explored and found to have inoperable disease. This makes a postoperative mortality rate of 19.5 per cent.

TABLE I

AGE DISTRIBUTION OF PATIENTS WITH CARCINOMA OF THE ESOPHAGUS AND STOMACH WHO WERE OPERATED UPON

Age	Entire Series	Resection Cases Only
30-40	5	2
40-50	23	17
50-60	37	28
60-70	35	26
70	13	7
Unknown	14	

(B) *Cases of Resection and Anastomosis*—Although the total group of radical operations numbers 86 cases, as was pointed out above, the 14 cases of midthoracic esophageal carcinoma in which the Torek operation was used are not included in this communication because of the entirely different technical problem involved and because the Torek procedure has been supplanted in all recent cases by resection and high esophagogastric anastomosis. Confining ourselves, therefore, to the radical resections followed by some form of anastomosis, 72 cases are available for study. Chart 2 summarizes the results of this experience.

There were 43 cases of carcinoma of the lower esophagus or of the fundus of the stomach invading the cardia in which a low esophagogastric anastomosis was performed. Eight of these patients died in the hospital (18.6 per cent). Of the 18 patients upon whom a total gastrectomy was performed, seven died in the hospital (38.8 per cent). In the midesophagus carcinoma group, where an anastomosis was performed, there were three deaths among 11 patients (27.2 per cent). Thus, of the entire group of 72 cases of radical resection followed by anastomosis, 18 patients died postoperatively. The over-all postoperative mortality rate therefore, was 25.0 per cent. Table II, which supplements Chart 2, indicates that of those who recovered following radical resection and anastomosis there were 13 patients whose convalescence was marred by complications of one sort or another. The total number of patients who manifested postoperative complications, obtained by adding together the number of deaths and the number of complicated cases ending in recovery, was 31, or 43 per cent. The total number of recoveries without complications was 41, or 67 per cent.

ANALYSIS OF THE COMPLICATIONS OCCURRING AFTER RESECTION

Table III gives a list of the principal complications which were recognized clinically or at autopsy. It must be remembered that in many cases several different complications occurred in the same patient so that the sum of the complications is greater than the total number of complicated cases.

RESULTS OF RESECTION AND ANASTOMOSIS IN 72 CASES OF CARCINOMA
OF THE STOMACH AND ESOPHAGUS

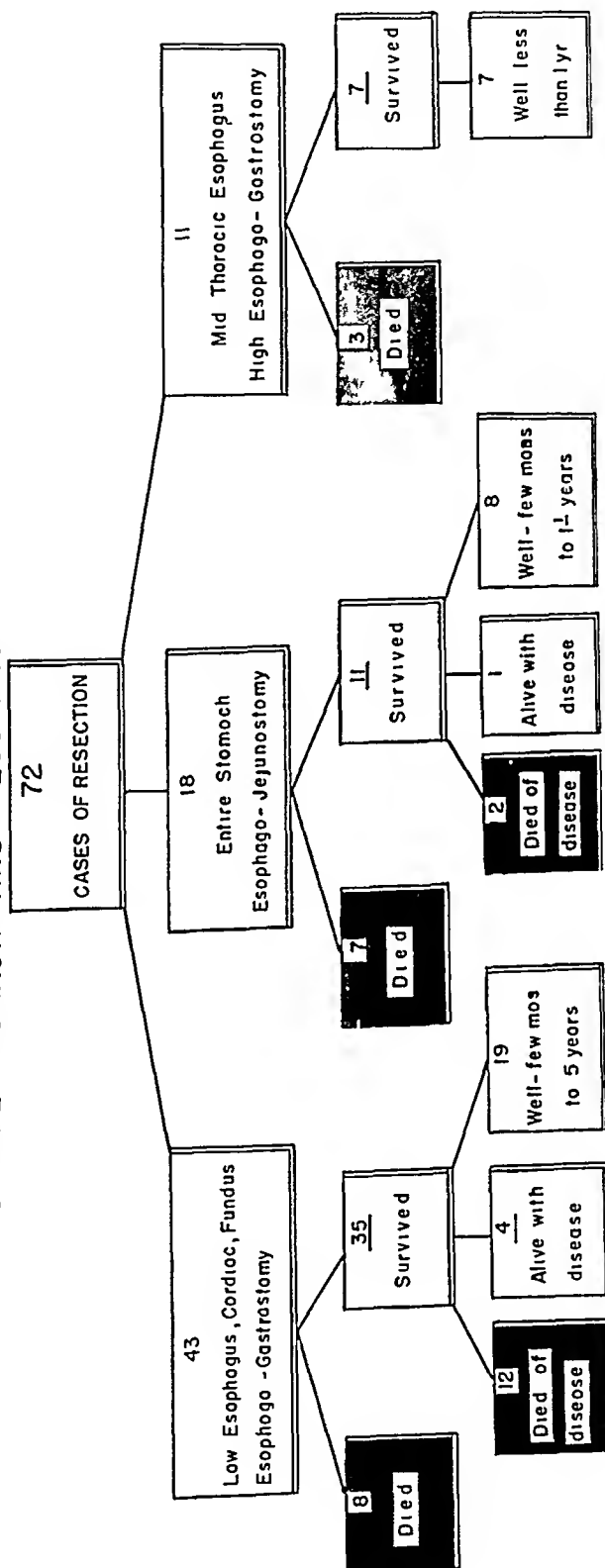


CHART 2

MANIFESTATIONS OF INFECTION — *Empyema* was observed in eight cases. It was a contributing cause of death in five of the patients who had a total gastrectomy. In all of these there was widespread sepsis with peritonitis, mediastinitis, or septic embolism, and the empyema was merely one aspect

TABLE II
IMMEDIATE RESULTS OF OPERATION

	No. of Cases	Deaths	Recovery with Complications	Recovery without Complications
Low esophagogastric anastomosis	43	8	10	25
Total gastrectomy	18	7	2	9
High esophagogastric anastomosis	11	3	1	7
Entire group	72	18	13	41

of the generalized infection. It occurred in three cases of resection of the cardia and fundus followed by a low thoracic esophagogastric anastomosis. All were operated upon before the year 1942, at a time when sulfanilamide was being used locally in the chest and before catheter drainage of the left pleural cavity was used routinely in all cases. Since then there have been no cases of empyema except in the total gastrectomy group. All three of these patients recovered after suitable drainage of the empyema was effected by rib resection.

Mediastinitis was recognized in four patients, as proven by autopsy examination. It may have occurred in others who recovered or upon whom no autopsy was performed. It was usually accompanied by other evidences of infection.

Peritonitis, as mentioned above, was found at autopsy in five patients who died of overwhelming sepsis after total gastrectomy.

Major wound sepsis occurred in two cases. In one of these there is little doubt that the patient's life was saved by the use of penicillin. The organism in this case was *staphylococcus aureus*.

Acute parotitis occurred in three cases, but in all of these the patient survived. In none was the patient extremely ill. All were bilateral.

CARDIAC DISORDERS — Table III enumerates the kinds of cardiac disorders encountered. Disturbances of rhythm without other cardiac signs were relatively infrequent, four cases in all. In three of these auricular fibrillation occurred and digitalization was of benefit. Auricular flutter occurred in one case and was of alarming seriousness. It was finally controlled by the administration of quinidine. Congestive failure of the heart was the principal or at least a major contributing cause of death in six patients. The majority of these had other complications as well, mostly sepsis. A diagnosis of myocardial infarction was made in three cases.

PULMONARY EMBOLISM — Massive pulmonary embolism occurred in four cases, representing an incidence of 5.5 per cent. In two of these sudden death resulted. In neither case was there any evidence of venous thrombosis in the

legs. One patient died while on her way to the front door of the hospital on the day she was to be discharged. The other died sitting in a chair the day before it had been planned to send her home. In the two other cases massive pulmonary emboli were found along with other complications when

TABLE III

ANALYSIS OF COMPLICATIONS WHICH DEVELOPED IN 72 PATIENTS IN WHOM A RESECTION WAS PERFORMED

	Low Anastomosis	High Anastomosis	Total Gastrectomy	Summary	Per Cent
Empyema	3 (no deaths) (2 operated upon)	0	5 (all died)	8	11.1
Mediastinitis	2	1	1	4	5.5
Peritonitis (usually with empyema, often with mediastinitis)	0	0	5	5	6.9
Major wound sepsis	1	1	0	2	2.8
Acute parotitis	2	0	1	3	4.2
Cardiac disorders					
Auricular fibrillation	2	1	0	3	4.2
Auricular flutter	1	0	0	1	1.4
Congestive failure	3	2	1	6	8.3
Myocardial infarction	1	2	0	3	4.2
Pulmonary embolism	1	0	3	4	5.5
Thrombophlebitis of femoral vein (requiring ligation)	0	0	2	2	2.8

an autopsy was performed. In one of these the patient was so ill because of sepsis, including empyema and peritonitis, that he would have died even if he had not suffered the embolism. Although pulmonary embolism was probably the immediate cause of death, this case was included in the group of deaths from sepsis. In none of these cases of pulmonary embolism was there warning beforehand or time enough after the embolism occurred to tie the femoral veins.

THROMBOPHLEBITIS OF THE FEMORAL VEIN requiring bilateral superficial femoral vein ligation occurred in two cases.

CAUSES OF DEATH AFTER OPERATION

In the entire series of 72 radical resections followed by some form of anastomosis (thus excluding the Torek operations) 18 postoperative fatalities occurred. The distribution of these fatalities according to the type of operation performed is shown in Table IV.

In the 18 fatalities an exact anatomic diagnosis of the cause of death was obtained by postmortem examination in 11 cases. In most of these there were several complicating factors, but in each it was possible to determine the principal cause. In the remaining seven cases the clinical diagnosis unconfirmed by autopsy is given.

Table V illustrates the principal causes of death arranged according to the type of operation performed. For the sake of brevity, in all those cases where the chief cause of death was infection of some type, the cause of death is ascribed to sepsis. In the majority of these there was widespread

overwhelming infection including often in the same case empyema (frequently bilateral), mediastinitis, peritonitis, pericarditis, septic infarcts of the liver, pancreatitis, and other foci. As was mentioned above, although massive pulmonary embolism occurred in four cases, it was thought to be the principal cause of death in only three. In the fourth case the embolism was probably the terminal event in a patient who was almost certain to die

TABLE IV

POSTOPERATIVE MORTALITY OF THIRTY TYPES OF OPERATION IN 72 CASES OF CARCINOMA OF THE ESOPHAGUS
CARDIA OR STOMACH

	No. of Cases	No. of Deaths	Per Cent
Resection with low esophagogastrostomy	43	8	18.6
Resection, with high esophagogastrostomy	11	3	27.3
Total gastrectomy, with esophagojejunostomy	18	7	38.9
Entire series	72	18	25.0

of sepsis. In the remaining cases the chief cause of death could almost certainly be ascribed to congestive cardiac failure (three cases) or to myocardial infarction (two cases).

The number of cases manifesting complications is too small to make any significant correlation between the type of operation or the location of the tumor and the nature of the complications which might occur. In the cases of carcinoma of the stomach requiring total gastrectomy, however, there was a much higher incidence of severe sepsis than in the other cases. This may have been the result of technical faults, but it would seem more likely that it was due to the fact that these patients were in a more depleted nutritional state than those who had less involvement of the stomach. During the past two years greater emphasis has been put upon the details of preoperative preparation of the patient and, possibly as a result of this, less trouble has been encountered.

COMMENTS REGARDING IMPROVEMENTS IN THE IMMEDIATE RESULTS OF OPERATION

Chart 3 serves to illustrate the fact that as a result of accumulated experience and the establishment of a now fairly standardized routine of preoperative preparation, operative technique, and postoperative care, the relative frequency of complications after operation and the percentage of postoperative deaths have fallen, especially during the years 1943 and 1944. Starting in 1939 with one operation, the number of radical resections has increased rapidly each year so that thus far in ten months of 1944 there have been 34 cases. At first, the number of cases attended by complications or resulting in death was roughly parallel with the total number of cases (Chart 3). But during 1943 and 1944 there has occurred a progressive decrease in the complicated or fatal cases and a relative increase in the survivors with or without complications. This reduction in the rate of occurrence of postoperative complications, whether fatal or not, cannot be ascribed to the operation of any one factor in the management of these

RESECTION OF ESOPHAGUS AND STOMACH

cases It is more certainly the result of the benefits resulting from the accumulation of experience with the difficult problems which are presented. In the early cases the preoperative preparation was not so intensive or so prolonged, and did not include the intravenous use of amino-acid preparations

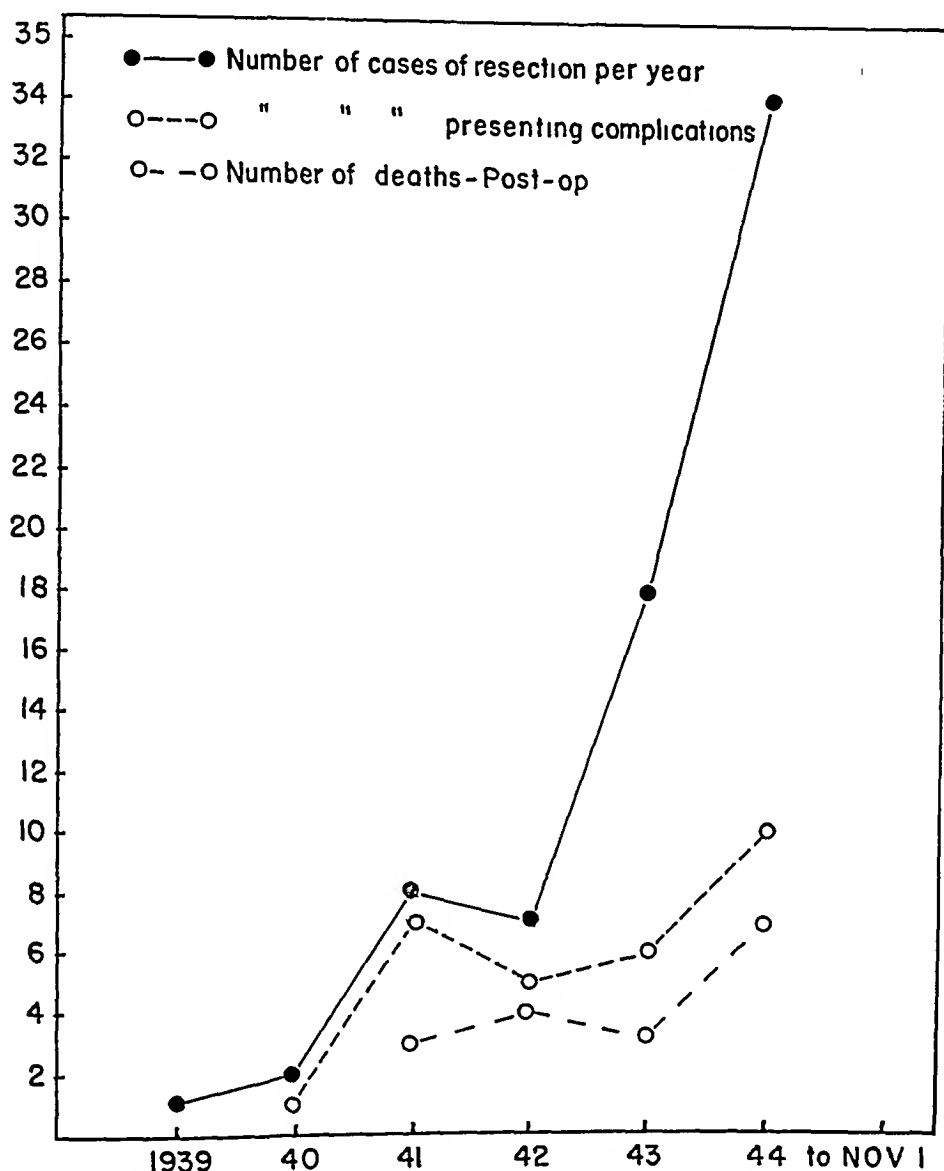


CHART 3—Number of cases of resection and anastomosis per year, starting in 1939 and including the first 10 months of 1944, number of complications and number of deaths each year

or the administration of sulfadiazene. The technic of operation has been modified very little, but now includes such things as the omission of the use of clamps on the esophagus, the utilization of routine drainage of the chest, and the avoidance, if possible, of splenectomy. In the postoperative care a much more thoroughly standardized procedure is followed. A summary of the factors which are considered of primary importance in the management of these cases follows:

(A) PRELIMINARY PREPARATION OF THE PATIENT—(1) Prolonged preoperative hospitalization of the patient (one to three weeks) to provide for

physical rest and thorough clinical and laboratory study to evaluate the patient's condition

TABLE V
CAUSES OF DEATH FOLLOWING RESECTION AND ANASTOMOSIS
ARRANGED ACCORDING TO TYPE OF OPERATION

	Sepsis	Congestive Failure	Pulmonary Embolus	Myocardial Infarction	Summary
Resection, with low esophagogastric anastomosis	4	3	1	0	8
Resection, with high esophagogastric anastomosis	1	0	0	2	3
Total gastrectomy with esophagojejunostomy	5	0	2	0	7
Entire series	10	3	3	2	18

(2) Transfusion of whole blood sufficient to restore the results of photo-hemoglobin determination to a normal level

(3) Administration of a high protein, high carbohydrate diet This in the obstructed cases must often be almost entirely liquid, for those who can take solid food a well-balanced diet is prescribed

(4) Exhibition of large doses of ascorbic acid (100 to 1000 mg) per day

(5) Exhibition of vitamin B-complex, usually in liquid form

(6) Digitalization in those with auricular fibrillation and in certain very elderly patients

(7) Routine administration of sulfadiazene, one gram every four hours for 48 hours preceding the day of operation

(8) Preliminary jejunostomy for feeding in a few patients who cannot swallow an adequate liquid or semisolid diet

(B) CONDUCT OF THE OPERATION —(1) The use of intratracheal positive pressure inhalation anesthesia (ether and oxygen)

(2) Routine complete expansion of the lung by the anesthetist every 20 to 30 minutes during the progress of the operation

(3) Transfusion of blood during the operation This is started as soon as the skin incision is made and two or three pints of blood are administered during the course of the procedure

(4) Use of silk technic throughout, including the anastomosis

(5) Avoidance of tying large masses of tissue

(6) Scrupulous hemostasis and particular care to avoid the development of hematomata in the mesentery or walls of viscera

(7) Avoidance of trauma to tissues, no clamps on the esophagus, no clamps for the anastomosis, no utilization of the cautery

(8) Avoidance of splenectomy when possible, (to prevent the development of splenic vein thrombosis and subsequent hepatic emboli) The spleen must be removed (a) if torn, (b) if adherent to the growth or if the growth invades the tissues around the splenic vessels, and (c) if it will lie in the way of the anastomosis (especially in those cases in which an esophagojejunostomy is performed)

- (9) Avoidance of the local utilization of sulfonamides, which would predispose to the development of empyema
- (10) Routine insertion of catheter for closed system drainage of the chest
- (11) Levin tube left with tip just above but not through the anastomosis
- (C) POSTOPERATIVE CARE — (1) Routine use of oxygen tent for 24 hours, or sometimes longer
- (2) Removal of Levin tube on the day after operation
- (3) Removal of chest drainage tube 48 to 72 hours after operation, depending upon the amount of drainage
- (4) Careful clinical observation twice each day to detect particularly,
 - (a) Tension pneumothorax
 - (b) Fluid in the chest
 - (c) Evidence of intrapulmonic disease (collapse or pneumonia)
 - (d) Cardiac arrhythmias
- (5) Aspiration of the chest if fluid is suspected
- (6) Routine portable chest roentgenogram on the 5th day, or at any other time if indicated
- (7) Daily administration of intravenous alimentation and medication of water with glucose or salt as indicated, aminogen if protein is low, vitamins (ascorbic acid, riboflavin, thiamine, and nicotinamide)
- (8) Oral feeding, begun on the 5th day, of water (one ounce) every hour, with a gradual increase in the amount and kinds of nutritious fluids and later soft solids, depending upon the toleration of the patient
- (9) Patient allowed out of bed on the 4th to 7th day
- (10) Sulfadiazene, five grams daily, continued for five days, or longer if necessary, to be omitted if signs of toxicity occur
- (11) Bilateral superficial femoral vein ligation and division if signs of deep phlebitis develop or after sublethal pulmonary embolism is detected

END-RESULTS AFTER RADICAL RESECTION FOLLOWED BY ANASTOMOSIS

Reference to Chart 2 demonstrates that of those who survived the operation some are already dead because of metastases or recurrence of the disease, a few are alive with recurrent disease, and some are apparently well. The seven survivors following resection of carcinoma of the midthoracic esophagus followed by a high esophagogastric anastomosis are all apparently well, but all were operated upon less than one year ago, so that one cannot attach much significance to their apparent good results. More of the total gastrectomy cases occurred long enough ago to give some impression of the end-result. But the largest and longest surviving group is composed of those who had resections of the cardia with a low thoracic esophagogastric anastomosis. Table VI gives the results to date in the 35 survivors after resection of the cardia with low esophagogastric anastomosis and the 11 patients who survived after total gastrectomy.

In the former group, 13 patients have been operated upon less than one year. Of these, three already show evidence of recurrent or metastatic

disease Seven of the 35 patients died less than one year after operation Fifteen patients survived one year, or longer But of these, one is alive, with recurrence, and four died from one year to 18 months after operation Eight

TABLE VI

35 CASES OF RESECTION OF CARCINOMA OF CARDIA				11 CASES OF TOTAL GASTRECTOMY		
Time Elapsed after Operation	Alive and Well	Alive, with Disease	Died of Recur- rence	Alive and Well	Alive with Disease	Died of Recur- rence
Less than 6 months	5	0	3	5	0	0
Six months to 1 year	5	3	4	1	1	2
1 year to 18 months	2	1	4	2		
18 months to 2 years	2	0	1			
2 to 3 years	2					
3 to 4 years	2					
4 to 5 years						
Over 5 years	1					
Total	19	4	12	8	1	2

patients survived more than 18 months One died before the expiration of two years, and two are alive and well a comparable length of time Two patients are well between two and three years postoperative Only three are alive and apparently well three or more years after operation One of these, the first case of the entire series, is well after five years

Obviously, too little time has elapsed since the operation in the majority of cases to get any accurate impression of what the end-results from the standpoint of survival are to be They will no doubt be disappointing if one expects to cure these patients But the importance of the operation as a method of palliation cannot be stressed too much A large percentage of these patients before operation cannot swallow enough food to keep from starving The happiness which results from being able to eat again is truly pathetic in many instances Furthermore, one should remember that not long ago the great majority of patients with carcinoma in the esophagus or cardiac end of the stomach would have been refused the benefit of surgery because lesions in these locations were considered by the majority of surgeons to be inoperable As a result of these factors I have adopted the policy of resecting every growth that can be removed even if the operation must be exceedingly radical, such as when it is necessary to remove a portion of the diaphragm, the spleen, the tail of the pancreas, or even portions of the left lobe of the liver If after such radical surgery the patient is relieved of his obstruction and can swallow satisfactorily again, if only for six months to one year, the operation should be considered worth while

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SELECTION OF THE TIME FOR GRAFTING OF SKIN TO EXTENSIVE DEFECTS RESULTING FROM DEEP THERMAL BURNS

H J McCORKLE, M D , AND HENRY SILVANI, M D

SAN FRANCISCO, CALIF

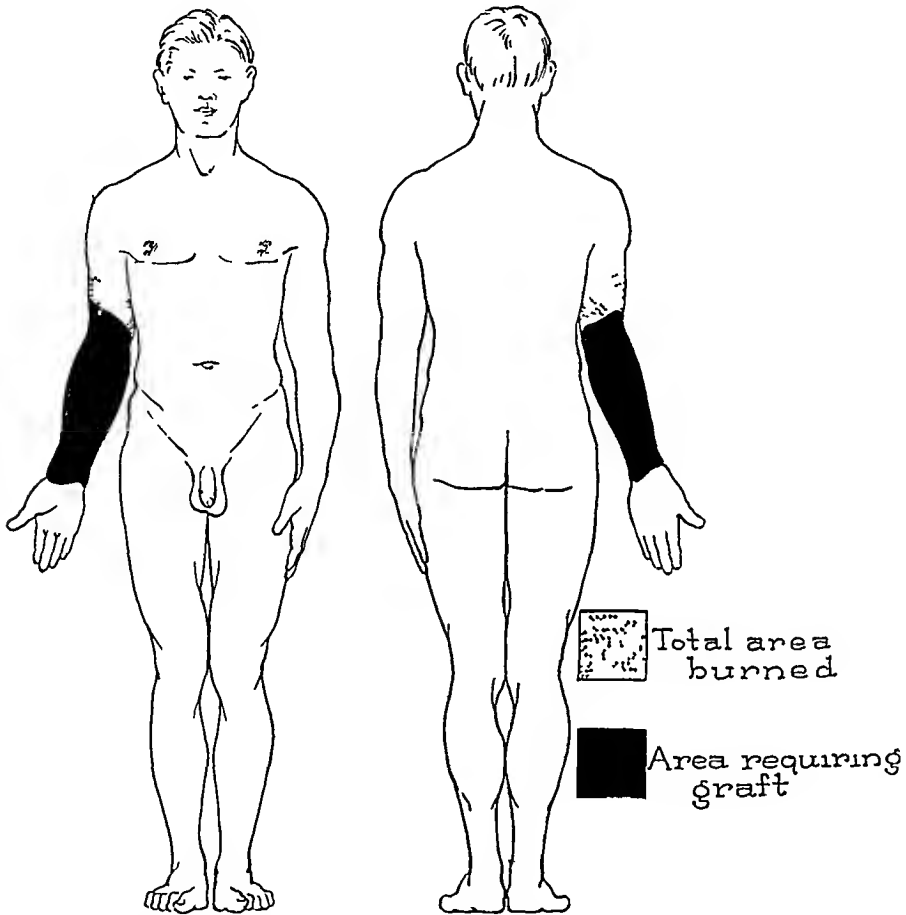
FROM THE DIVISION OF SURGERY, UNIVERSITY OF CALIFORNIA MEDICAL SCHOOL SAN FRANCISCO CALIF

LARGE AREAS that have been deeply burned should be covered with epithelium by means of skin grafts at the earliest suitable opportunity. It is necessary, however, to wait until shock, alterations in body proteins, fluid and electrolyte balance, renal function, edema "toxemia," etc, have been controlled. Also, it is desirable to delay the grafting until the epithelium has been restored spontaneously to all areas of second degree burn. To wait for large full-thickness defects to epithelize, however, even though they contain small viable epithelial islands that eventually might spread to cover the area, is usually unwise. Grafting should be done early enough to avoid the period of debilitation so often associated with the presence of large granulating areas several weeks after a severe burn. Such areas are prone to become infected, bleeding, exuding and painful, and lead to extensive loss of protein and other serious nutritional deficiencies, sepsis, emaciation and poor morale. Maintenance of nutrition, with particular reference to a diet high in protein and vitamin C, is essential, especially if early skin grafting is contemplated. Though early grafting may be done successfully in the presence of mild localized infection, extensive, spreading or disseminated infection must be controlled before deeply burned areas can be covered with skin. Infrequent dressings done with aseptic precautions and supplemented by chemotherapy are valuable adjuncts in controlling or minimizing infection.

It is difficult to designate an exact time that will satisfy all of these requirements. Some time between the fourteenth and twenty-first days after the burn often will be found to fulfill most of them. The most difficult problem in this particular period is the removal of the burned tissues from those which are viable, in order to obtain a surface suitable for the application of skin grafts. Many weeks are likely to be required for the autolization or spontaneous casting off of the tissue destroyed by the burn. The elimination of such tissues has been hastened somewhat by employing chemicals such as Dakin's solution and more recently by the use of enzymes^{3, 5} or the pyruvic acid method². An alternative method is their removal by surgical excision^{1, 4, 6}. This should be done in a fully equipped operating room, preferably at some time between the second and third weeks following the burn. The procedure of excision of burned tissues and early skin grafting may be used both for burned patients treated initially with a compression type of dressing and those upon whom coagulum-producing drugs such as

tannic acid-silver nitrate or the dyes were used. A general anesthetic is required.

The burned area and surrounding skin are cleaned thoroughly with a detergent solution and draped with sterile linens. The proposed donor areas are prepared similarly, but separately. All necrotic tissue is excised, preserving as much viable tissue as is possible. The oozing of blood may be considerable, but is not dangerous if it is kept under control continually.



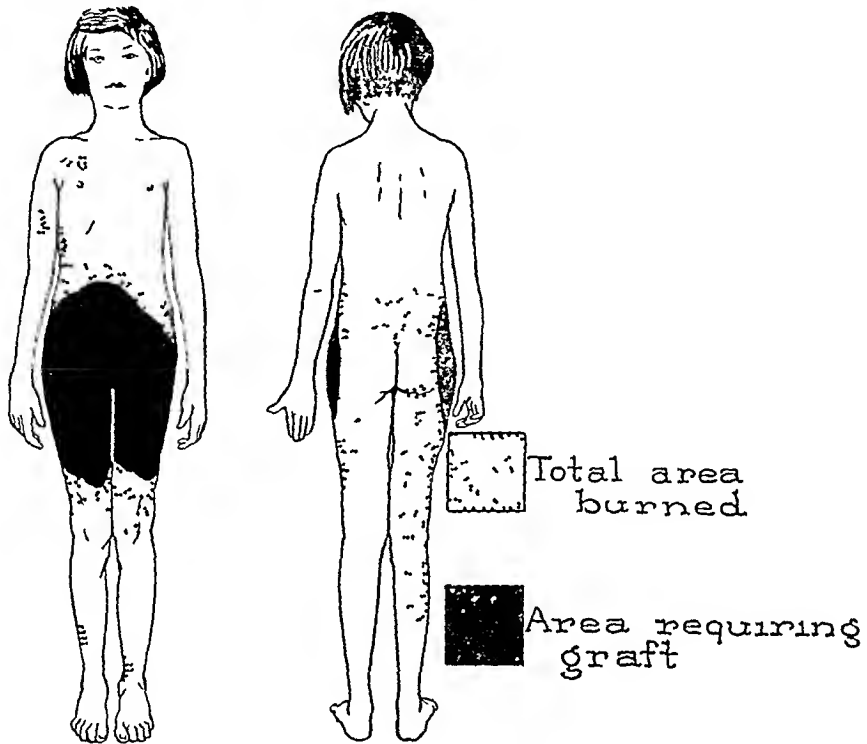
I N Male Age Burned by hot coffee
Hospital stay 7 weeks

FIG 1

by pressure applied with warm saline sponges. Occasionally a few ligatures may be required to control actively bleeding vessels. During the dissection of coagulum and nonviable tissue care must be taken to minimize injury to remaining viable tissues. This dissection is difficult and slow. It is preferable to apply skin grafts at the same operation if the condition of the patient permits, but occasionally it may be necessary to delay for a few days before placing the grafts at a second operation.

Skin grafts of intermediate thickness are removed from donor sites, using the Padgett or Blair method, and are fixed to the denuded areas with cotton

sutures If the available donor sites do not provide enough grafts to cover the deficient areas completely, the grafts are cut into small squares ("postage stamps"), from 1.5 to 2 cm in size, and are placed as near to one another as is possible over the entire defect, but they are not sutured. Donor and grafted areas are covered with a single layer of fine-mesh gauze impregnated with a grease base containing a bland antiseptic ointment and voluminous compression dressings are applied. In children or in adults



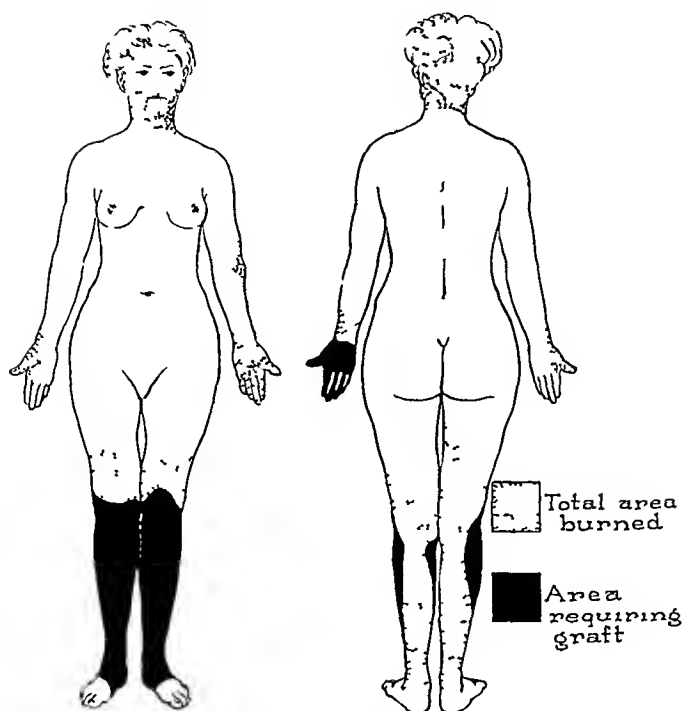
ET Female Age 9 Dress caught on fire
Hospital stay 12 weeks

FIG 2

with burns near joints a light plaster covering may be placed over the compression dressing. If possible, the original dressings are left in place for two weeks following the grafting procedure, if it becomes necessary to remove them earlier, the procedure should be done in the operating room, and a compression dressing should be reapplied at once.

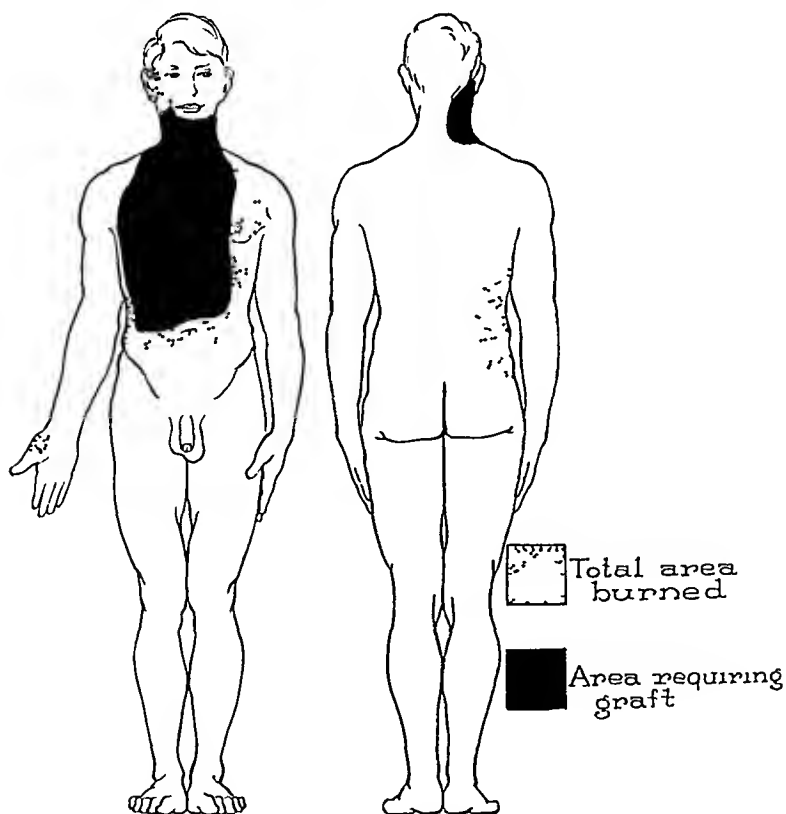
Usually the areas that were fully covered with grafts will be healed by about the fourteenth day, but "postage stamp" areas require longer periods for complete epithelization and should be redressed until they are entirely healed. Occasionally supplementary skin grafting may be required. Grafted areas must be protected from injury for several weeks or months.

Over a period of one year (July 1, 1942, to June 30, 1943) patients who suffered deep burns of the skin of various parts of the body were treated as described above. The burned surfaces were debrided and grafted with skin (during the second or third week) after the injury. The burns varied in extent from two to 32 per cent of the body surface. The total period of hospitalization for this group of patients varied from five to 12 weeks.



EM Female Age 17 Burned in auto accident
Hospital stay—8 weeks

FIG 3

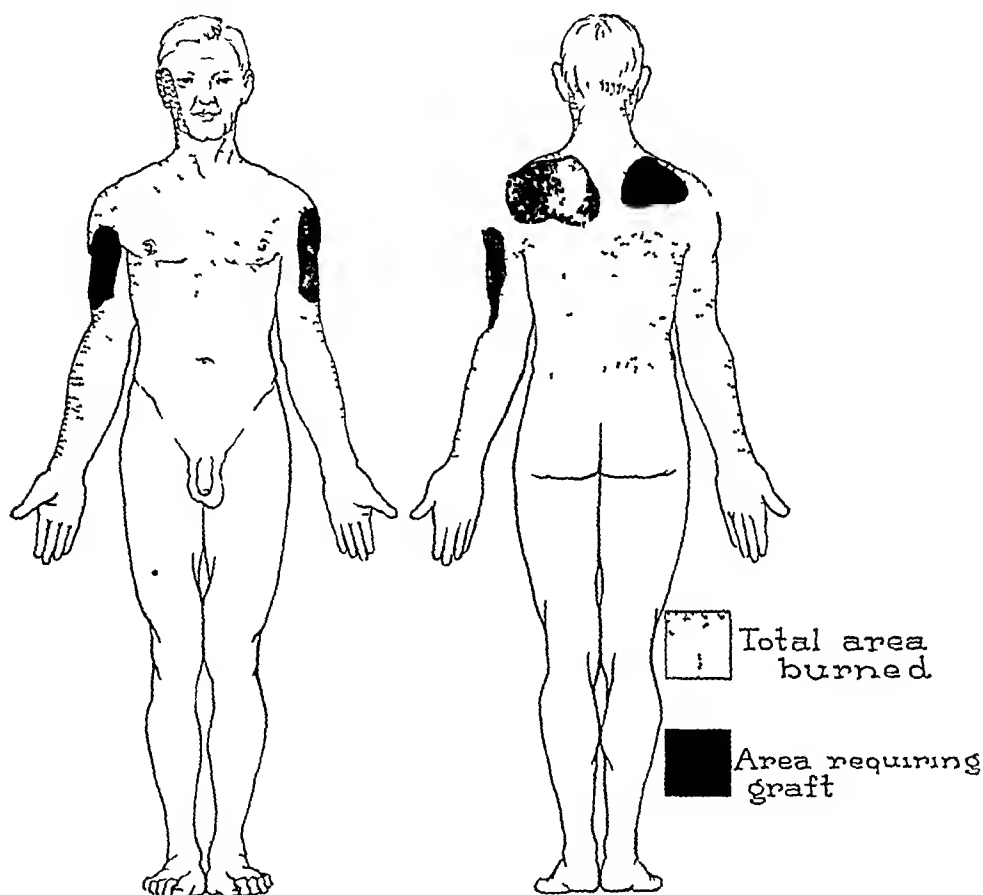


L McC Male Age 28 Burned in bed
Hospital stay 8 weeks

FIG 4

and averaged six and one-half weeks. Figures 1 to 5 indicate the location and extent of the injury in some of these cases.

Apparently, early grafting of skin following extensive deep burns minimizes contracture and deformity. Some patients will need no additional procedures, but others will require plastic correction of contractures that have resulted in spite of early grafting. For such patients the early closure of burn wounds by the application of grafts of intermediate thickness probably will permit earlier plastic repair.



R.M. Male Age 43 Burned when bed caught on fire
Hospital stay 8 weeks

FIG 5

SUMMARY

A period somewhere between the second and third weeks after an extensive deep thermal burn is likely to prove the optimum time for excision of nonviable burned tissues and the immediate application of skin grafts of intermediate thickness. The dissection is difficult and small amounts of viable tissues may be removed inadvertently. On the other hand, morbidity is reduced considerably, and recovery apparently is earlier.

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THE INFLUENCE OF LOCAL TREATMENT OF BURNS ON LIVER FUNCTION

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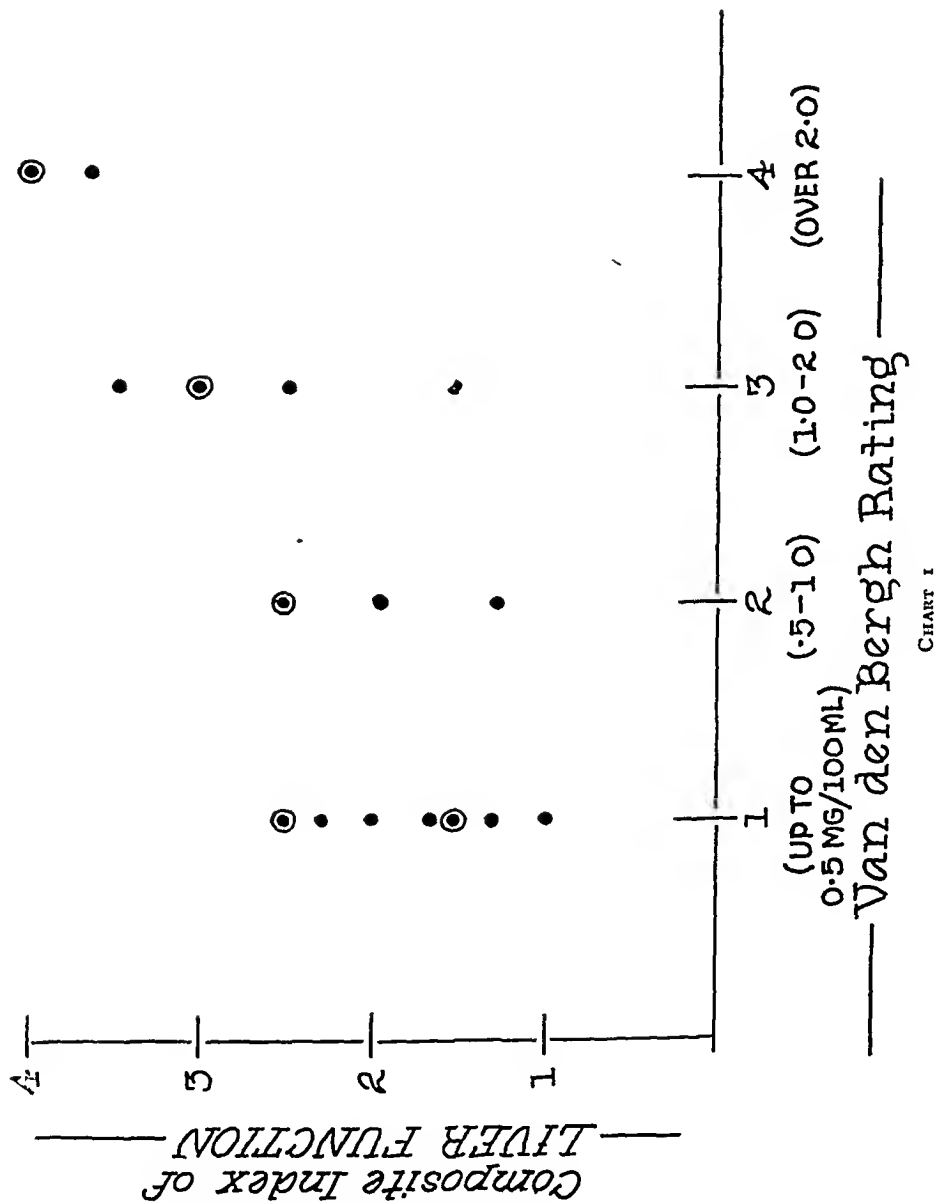
THE RELATION OF LOCAL TREATMENT of burns to hepatic damage has been approached in the past either by animal experiments^{1, 2, 3} or by a study of the pathologic changes found in fatal cases at autopsy⁴

The present study has been concerned primarily with the functional changes in the liver. Most of the patients studied survived. It is important not only to determine the effect on liver function of tannic acid but also of other tanning agents. Two other questions are of considerable interest. First, is the hepatic damage following the use of tannic acid locally a cause of increased mortality? Second, is the hepatic damage following burns entirely due to therapeutic agents used in the local treatment of the burned areas?

Plan of Study—Burned patients admitted to the Pennsylvania Hospital on the service of Dr. W. E. Lee had been the subject of intensive study for several years,^{5, 6} and preliminary observations on liver function tests were reported in 1940.⁵ From September 1, 1941, to December 31, 1942, a study on the use of adrenal cortical extract in burn therapy⁷ was carried out under an Office of Scientific Research and Development contract. The clinical material was made available by seven Philadelphia hospitals. This work was done entirely on patients whose burns were treated locally either with tannic acid or one of the other tanning agents. From January 1, 1943, until June 30, 1944, a study directed primarily at liver function was carried out under an Office of Scientific Research and Development contract on a group of patients admitted to 11 hospitals in the Philadelphia area, and most of these patients were treated locally with petrolatum gauze and pressure dressings.

The four liver function studies used in this work were not done on many of the earlier patients but van den Bergh determinations were followed in most of them and the group studied in 1943-1944 provided a good opportunity to compare the results of the four liver function tests on a large number of patients. It was found that the results of different tests in a given patient were often at variance but that a combination of the van den Bergh test, the bromsulphalein retention, the hippuric acid conjugation test and the cephalin flocculation test gave an index that was fairly well correlated with the results of the van den Bergh test (Chart 1).

Methods—Blood specimens were collected in Sanford-Magath hematocrit tubes with small amounts of powdered heparin or sodium oxalate. The tubes



LIVER FUNCTION IN BURNS

TABLE I
LIVER FUNCTION TESTS IN PATIENTS TREATED WITH TANNING METHODS

Patient	Age	% Area Burned	Local Treatment	Survival	van den Bergh	% Bromsulphalein	Hippuric Acid
C A	9	65	Tannic acid	Died 5th day	1 0		
T A	5	25	Tannic acid	Yes	0 7	24	1 22
A L	50	40	Gentian violet	Died 4th day	4 8		
			Silver nitrate				
E S	14	18	Tannic acid	Yes	0 5		
M H	12	20	Tannic acid	Yes	0 7		
P M	56	15	Gentian violet	Yes	0 7		
			Silver nitrate				
E R	40	15	Gentian violet	Yes	1 8		
			Silver nitrate				
R V	6	15	Tannic acid	Yes	1 2		
R D	50	40	Sulfathiazole ointment	Yes	0 5		
E F	3	35	Gentian violet	Yes	1 5		
			Silver nitrate				
O B	17	40	Tannic acid	Died 5th day	16 8		
			Gentian violet				
			Silver nitrate				
B A	35	15	Gentian violet	Yes	0 9		3 98
			Silver nitrate				
R B	42	20	Petrolatum	Yes	0 6		
R B	6	15	Triple dye	Yes	5 4		
R M B	4	25	Pickrell's solution	Yes	0 1		trace
C E	33	25	Tannic acid	Yes	2 3	33	3 17
			Silver nitrate				
R C	37	70	Tannic acid	Died	1 2	4	4 00
			Silver nitrate				
J P	44	15	Gentian violet	Yes	1 2	17	2 09
J P	23	20	Gentian violet	Yes	2 0	17	1 47
W M		20	Gentian violet	Yes	0 4	10	2 46
			Silver nitrate				
L H	66	50	Gentian violet	Died 40th day	2 9	10	
			Silver nitrate				
M K	19	90	Tannic acid	Died 3rd day	13 0		
			Silver nitrate				
G S	4	15	Gentian violet	Yes	0 3		
			Silver nitrate				
J G	23	22	Gentian violet	Yes	0 8	4	2 04
			Silver nitrate				
H G	63	15	Petrolatum	Yes	0 7		
			Sulfathiazole				
A W	38	20	Triple dye	Yes	1 2		
H Mc	27	16	Tannic acid	Yes	1 4		
			Gentian violet				
P G	55	45	Triple dye	Died 8th day	1 3		
L M	13	20	Tannic acid	Died 6th day	11 0		
F H	40	40	Tannic acid	Died 20th day	1 0		
N C	8	15	Gentian violet	Yes	0 3		
			Silver nitrate				
T K	39	90	Triple dye	Died 19th hour	4 9		
I M W	1	35	Gentian violet	Yes	1 0		
			Silver nitrate				
L W	22	22	Gentian violet	Yes	1 3		2 99

were centrifuged within an hour of taking the blood and the supernatant plasma drawn off

Serum bilirubin levels were determined by the indirect van den Bergh reaction,^{8, 9} using potassium permanganate solutions as the colorimetric standard. These determinations were run within ten hours of the taking of the blood, and in all cases the serum or plasma was removed from contact with the cells within one hour.

TABLE II

ARBITRARY VALUES USED IN GRADING THE SEVERITY OF LIVER DAMAGE ACCORDING TO THE VARIOUS TESTS

	van den Bergh	Bromsulphalein % Retention at 30 Minutes	Cephalin Flocculation	Hippuric Acid Conjugation
Grade I (normal)	Up to 0.5 mg per 100 Ml	Up to 2	0	1.0 Gm or above
Grade 2 (mild damage)	0.5-1.0 mg per 100 Ml	2-5	1 plus	1.0-0.85 Gm
Grade 3 (moderate damage)	1.0-2.0 mg per 100 Ml	5-15	2 plus	0.85-0.75 Gm
Grade 4 (marked damage)	Above 2.0 mg per 100 Ml	Over 15	3 or 4 plus	Less than 0.75 Gm

The ability of the liver to excrete bromsulphalein was measured^{10, 11} A standard dose of 5.0 mg per kilogram of body weight was injected intravenously. One-half hour later a specimen of blood was withdrawn from a vein other than that used for injection of the dye to avoid error due to adsorption of bromsulphalein by the intima of the vessel.

The ability of the liver to conjugate the benzoic acid with glycine was measured after the method of Quick^{12, 13} Immediately after the patient had voided, 1.77 Gm of sodium benzoate in 20 cc of solution was injected intravenously over a five- to ten-minute period of time. One hour later the urinary output of the hour was collected. In occasional patients the oral route of administration was used, giving 6 Gm of sodium benzoate orally in 30 cc of water and collecting the urine for the succeeding four hours.

The cephalin flocculation of serum was determined, as outlined by Hanger^{14, 15}

Carboxyl nitrogen, representing the amino-nitrogen of the *alpha* amino-acids, was determined on plasma, following the method of MacFadyen¹⁶

Plasma proteins were measured by the falling-drop determination of specific gravity, as described by Barbour and Hamilton¹⁷ Some protein concentrations and the albumin-globulin ratios were determined by the biuret method^{18, 19}

Results—In the series of 38 patients studied prior to 1943, 34 were treated with tanning methods locally. Serum bilirubin levels were determined by the van den Bergh test in all these cases, and the results are presented in Table I, as well as a few determinations of liver function by other means. Owing to the fact that the tannic acid treatment had been replaced by other methods of treatment we have not had an opportunity to add to the tannic acid series since January 1, 1943. The 24 cases treated in 1943, presented in Table III, and the 23 cases treated in 1944 (Table IV) have been treated with open methods.

TABLE III
RESULTS OF LIVER FUNCTION TESTS
(1943 — Vaseline Gauze and Pressure Dressings)

No	Patient	Age	Survival Time	% Area Burned	% Hemato- crit	van den Bergh	Bromsulphalein % Retention at Rating 30 Minutes	Hippuric Acid Secretion Gm	Rating	Cephalin Flocculation	Rating	Com- posite Index
1	J H	5	Recovered	15	50	0 9	1	1	2	0	1	1 30
3	E N	10	5 days	45	48	1 3	3		3	+++	4	3 50
4	C R	52	Recovered	18	60	2 1	4		4	+++	3	3 66
11	H O	40	Recovered	20	63	0 7	2	33	2	++	3	2 60
22	C S	60	37 hours	35	53	3 2	4	27	4	++		4 00
23	E P	50	6 days	60	46	2 2	4	45	4	+++	4	4 00
24	S D	34	6 days	60	51	1 5	3		3	+++		4 00
25	D B	50	45 days	55	55	1 8	3	20	4	+++	3	3 00
26	J C	9	36 hours	60	50	0 4	1		1	++	1	2 60
34	D T	20	Recovered	25		0 1	1	3	2	++	2	1 50
35	V P	21	Recovered	20		0 4	1	1	1	0	1	1 30
37	G J	53	Recovered	25	43	0 5	1	8	3	+++	3	1 60
38	J Z	37	Recovered	20	50	1 7	3			+++		2 30
40	L B	21	Recovered	30		0 7	2	7	3	+	4	3 00
41	G L	10	Recovered	18	38	0 5	1		1	++	3	2 50
44	J C	39	Recovered	20	47	1 0	3	1	1	+		2 00
45	E L	42	3 days	35	55	0 2	1			0	1	1 60
18	C O	48	Recovered	18	45	0 5	2			+++	4	2 50
49	A S	31	3 5 days	50	50	0 4	1			+++	4	2 00
50	H R	52	Recovered	15	37	0 1	1	1	1	+++	3	2 50
51	C D	69	6 hours	50	44	0 2	1			+++		1 60
												1 00

The results of the tests of liver function on the 1943 series (Table III) were combined into an index of liver function by arbitrarily grading the maximum aberration from normal found by each test in a given case in accordance with the schedule in Table II. These grades or ratings were then

TABLE IV
RESULTS OF LIVER FUNCTION TESTS
(1944 - Patients)

No	Patient	Age	% Area Burned	Local Treatment	Survival	van den Bergh
1	G S	11	18	Saline	Yes	0 2
3	J L	6	15	Saline	Yes	0 6
4	A H	46	30	Petrolatum and pressure dressings	Died	0 8
					11th day	
5	W C	38	25	Petrolatum and pressure dressings	Yes	1 5
6	I M	38	18	Petrolatum and pressure dressings	Yes	0 3
7	V Y	42	55	Petrolatum and pressure dressings	Died	4 0
					62nd day	
8	D D	50	15	Petrolatum and pressure dressings	Yes	0 1
10	E E	6	30	Petrolatum and pressure dressings	Yes	1 0
11	M B	50	35	Petrolatum and pressure dressings	Yes	0 3
12	D G	27	35	Petrolatum and pressure dressings	Yes	1 2
19	C C	44	45	Triple dye	Died	2 1
					4th day	
21	M C	28	30	Petrolatum and pressure dressings	Died	0 3
					4th day	
25	M V	50	30	Petrolatum and pressure dressings	Yes	0 3
26	T S	22	18	Open	Yes	0 8
27	J S	4	18	Petrolatum and pressure dressings	Yes	0 2
28	R P	60	15	Petrolatum and pressure dressings	Yes	0 3
33	J N	58	20	Petrolatum and pressure dressings	Yes	1 0
34	E W	42	20	Petrolatum and pressure dressings	Yes	0 7
36	J G	60	60	Petrolatum and pressure dressings	Died	0 7
					1st day	
37	E H	58	75	Petrolatum and pressure dressings	Died	0 3
					1st day	
38	D Q	43	40	Petrolatum and pressure dressings	Died	0 3
					2nd day	
44	A S	72	35	Petrolatum and pressure dressings	Died	2 5
					5th day	
47	R K	15	18	Petrolatum and pressure dressings	Yes	1 7
48	E R	36	15	Petrolatum and pressure dressings	Yes	0 3

TABLE V
MAXIMUM PLASMA BILIRUBIN CONCENTRATION OBSERVED IN PATIENTS WITH BURNS
AFTER VARIOUS METHODS OF TREATMENT

Method	Total Cases	Average Area Burned	0-0.5 mg per 100 ml		0.5-2.0 mg per 100 ml		Over 2.0 mg per 100 ml		Mortality %
			No	%	No	%	No	%	
Tannic acid (either alone or combined)	14	33	1	7	9	64	4	29	21.4
All other tanning methods	20	28	5	25	12	60	3	15	20.0
Vaselined gauze with or without pressure dressings	47	31	22	47	20		5		33.7

averaged for each patient and the average called the composite index of liver function. Chart I shows the close correlation between the rating for the van den Bergh and the composite index. For this reason we believe the experience prior to 1943 with tanning methods can fairly be compared with later experience using open methods of treatment on the basis of serum bilirubin levels alone.

Table V shows an analysis of the van den Bergh tests obtained in the cases treated with tanning methods and open methods listed in Tables I,

III and IV In each case the highest bilirubin level is recorded We eliminated all burns from the series which covered less than 15 per cent of the body surface with the exception of two tannic acid cases in order to give a comparable series of cases Thus the average area for the cases treated with tannic acid is 33 per cent, for the cases treated with other tanning methods 28 per cent, and for the cases treated with open methods 31 per cent

The incidence of serum bilirubin levels above 2.0 mg per 100.0 MI was decidedly higher in the patients treated with tanning methods than in those treated with open methods The 14 cases treated with tannic acid had a still higher incidence of hyperbilirubinemia over 2.0 mg per 100.0 MI The influence of tannic acid in causing liver damage is even more clearly demonstrated by the following facts Although the tannic acid group comprises only 17 per cent of the total number of cases, yet all three patients having serum bilirubin levels over 10.0 mg per 100.0 MI fall in this group, and four out of the six patients having levels above 4.0 mg per 100.0 MI fall in this group

The general mortality of the untanned group was 33.7 per cent, as compared with 20.7 per cent for those treated with one or more of the tanning methods

The variations between clinical burns make any attempt at comparison difficult We have been impressed with the fact that the damage incurred by a severely burned patient is widespread, and that liver damage is perhaps more apt to be a contributing than a determining cause of death

Other Liver Function Tests—The carbohydrate tolerance tests were not employed in this series except in the small group previously reported,⁵ in which dextrose tolerance was studied Here, it was recognized that marked aberrations occurred but that interpretations were difficult Not only the liver but also pancreas, adrenal and pituitary might have been involved

Three other tests were employed, the bilirubin clearance test as described by von Bergmann and Eilbott, and modified by Jankelson and Gargill,²⁰ the carboxyl nitrogen and the albumin-globulin ratio The first was carried out on a small group of patients, and while consonant with the other tests it did not give promise of being unusually sensitive The determination of carboxyl nitrogen was suggested to us by C. N. H. Long, who had found it of value in experiments on rats In patients, however, it proved relatively insensitive and was only significantly elevated in seven out of 52 cases in which it was employed

The albumin-globulin ratios tended to become reversed in the latter part of the recovery period, usually after two or three weeks Furthermore, it seldom returned to normal until the local loss of protein-containing material from the surface of the wound ceased It, therefore, seems proper to regard the albumin-globulin ratio as an index of the patient's nutritional status rather than as purely an index of liver function It may be affected by hepatic damage also, but it did not follow the trend of the other liver function tests in the burned patient

Discussion—The selection of liver function tests is difficult since the

The results of the tests of liver function on the 1943 series (Table III) were combined into an index of liver function by arbitrarily grading the maximum aberration from normal found by each test in a given case in accordance with the schedule in Table II. These grades or ratings were then

TABLE IV
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(1944 - Patients)

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6	I M	38	18	Petrolatum and pressure dressings	Yes	0 3
7	V Y	42	55	Petrolatum and pressure dressings	Died 62nd day	4 0
8	D D	50	15	Petrolatum and pressure dressings	Yes	0 1
10	E E	6	30	Petrolatum and pressure dressings	Yes	1 0
11	M B	50	35	Petrolatum and pressure dressings	Yes	0 3
12	D G	27	35	Petrolatum and pressure dressings	Yes	1 2
19	C C	44	45	Triple dye	Died 4th day	2 1
21	M C	28	30	Petrolatum and pressure dressings	Died 4th day	0 3
25	M V	50	30	Petrolatum and pressure dressings	Yes	0 3
26	T S	22	18	Open	Yes	0 8
27	J S	4	18	Petrolatum and pressure dressings	Yes	0 2
28	R P	60	15	Petrolatum and pressure dressings	Yes	0 3
33	J N	58	20	Petrolatum and pressure dressings	Yes	1 0
34	E W	42	20	Petrolatum and pressure dressings	Yes	0 7
36	J G	60	60	Petrolatum and pressure dressings	Died 1st day	0 7
37	E H	58	75	Petrolatum and pressure dressings	Died 1st day	0 3
38	D Q	43	40	Petrolatum and pressure dressings	Died 2nd day	0 3
44	A S	72	35	Petrolatum and pressure dressings	Died 5th day	2 5
47	R K	15	18	Petrolatum and pressure dressings	Yes	1 7
48	E R	36	15	Petrolatum and pressure dressings	Yes	0 3

TABLE V
MAXIMUM PLASMA BILIRUBIN CONCENTRATION OBSERVED IN PATIENTS WITH BURNS
AFTER VARIOUS METHODS OF TREATMENT

Method	Average		0 0-0 5 mg		0 5-2 0 mg		Over 2 0 mg		Mortality
	Total Cases	Area Burned	per 100 Ml No	%	per 100 Ml No	%	per 100 Ml No	%	%
Tannic acid (either alone or combined)	14	33	1	7	9	64	4	29	21 4
All other tanning methods	20	28	5	25	12	60	3	15	20 0
Vaselined gauze with or without pressure dressings	47	31	22	47	20		5		33 7

averaged for each patient and the average called the composite index of liver function. Chart I shows the close correlation between the rating for the van den Bergh and the composite index. For this reason we believe the experience prior to 1943 with tanning methods can fairly be compared with later experience using open methods of treatment on the basis of serum bilirubin levels alone.

Table V shows an analysis of the van den Bergh tests obtained in the cases treated with tanning methods and open methods listed in Tables I,

III and IV In each case the highest bilirubin level is recorded We eliminated all burns from the series which covered less than 15 per cent of the body surface with the exception of two tannic acid cases in order to give a comparable series of cases Thus the average area for the cases treated with tannic acid is 33 per cent, for the cases treated with other tanning methods 28 per cent, and for the cases treated with open methods 31 per cent

The incidence of serum bilirubin levels above 2.0 mg per 100.0 Ml was decidedly higher in the patients treated with tanning methods than in those treated with open methods The 14 cases treated with tannic acid had a still higher incidence of hyperbilirubinemia over 2.0 mg per 100.0 Ml The influence of tannic acid in causing liver damage is even more clearly demonstrated by the following facts Although the tannic acid group comprises only 17 per cent of the total number of cases, yet all three patients having serum bilirubin levels over 10.0 mg per 100.0 Ml fall in this group, and four out of the six patients having levels above 4.0 mg per 100.0 Ml fall in this group

The general mortality of the untanned group was 33.7 per cent, as compared with 20.7 per cent for those treated with one or more of the tanning methods

The variations between clinical burns make any attempt at comparison difficult We have been impressed with the fact that the damage incurred by a severely burned patient is widespread, and that liver damage is perhaps more apt to be a contributing than a determining cause of death

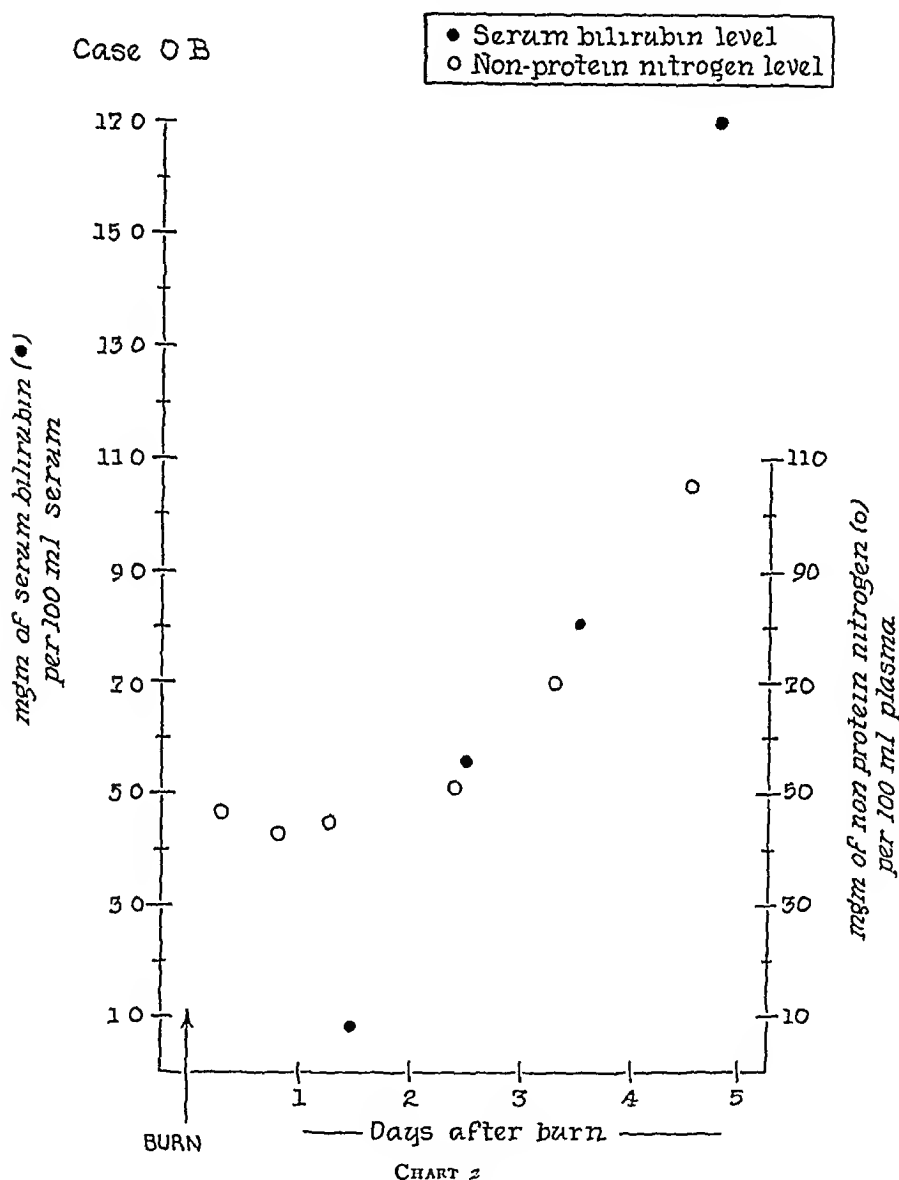
Other Liver Function Tests—The carbohydrate tolerance tests were not employed in this series except in the small group previously reported,⁵ in which dextrose tolerance was studied Here, it was recognized that marked aberrations occurred but that interpretations were difficult Not only the liver but also pancreas, adrenal and pituitary might have been involved

Three other tests were employed, the bilirubin clearance test as described by von Bergmann and Eilbott, and modified by Jankelson and Gargill,²⁰ the carboxyl nitrogen and the albumin-globulin ratio The first was carried out on a small group of patients, and while consonant with the other tests it did not give promise of being unusually sensitive The determination of carboxyl nitrogen was suggested to us by C. N. H. Long, who had found it of value in experiments on rats In patients, however, it proved relatively insensitive and was only significantly elevated in seven out of 52 cases in which it was employed

The albumin-globulin ratios tended to become reversed in the latter part of the recovery period, usually after two or three weeks Furthermore, it seldom returned to normal until the local loss of protein-containing material from the surface of the wound ceased It, therefore, seems proper to regard the albumin-globulin ratio as an index of the patient's nutritional status rather than as purely an index of liver function It may be affected by hepatic damage also, but it did not follow the trend of the other liver function tests in the burned patient

Discussion—The selection of liver function tests is difficult since the

liver plays an important role in so many metabolic processes. In addition, the liver has a large reserve and rapid powers of regeneration, so that much liver damage may occur before any of the function tests are affected. We have used the van den Bergh, the bromsulphalein retention, the hippuric



acid excretion and flocculation of cephalin-cholesterol emulsions in this series of patients.

Tannic acid was so well established in burn therapy that it, or one of the other tanning methods, had largely displaced other methods of local therapy in this country and to a considerable extent abroad. Emphasis on its hepatotoxic properties, by Wells, and his coworkers,^{1,2} came at a time when the visceral changes following burns were becoming of increasing importance, probably as the result of improvements in the treatment of shock. The difficulty of applying Well's observations in animals directly to human burns lies partly in the difference between injection and surface

absorption. The experimental animals, with the exception of fowl, do not blister, so that their burns are not comparable to human burns, and even the denudation experiments of Baker and Handler²¹ on rabbits' ears are not strictly comparable.

However, taken in conjunction with the autopsy data, reported by Eib, Farmer and Morgan,⁴ there can be little doubt that the tannic acid used in burn therapy is absorbed sufficiently to increase the hepatic damage. The data on liver function, which has been obtained in the Philadelphia cases reported above, is additional evidence in the same direction. Tannic acid is much the most hepatotoxic agent, but the other tanning methods are followed by much more disturbance than the nontanning methods. This is in close agreement with the toxicologic study of Hartman and Romence.³

The mildness of the changes in hepatic function seen in most of the cases treated locally by Koch's method is very gratifying, and while the changes are still definite it would seem that the predominance of hepatic damage in burn toxemia, as described by Wilson, McGregor and Stewart,²² and Pack,²³ has been largely due to tanning agents. At present we believe some degree of hepatic damage is the rule in the toxemia of burns, but it is usually a minor part of the picture.

The question of whether tannic acid actually caused the deaths of burned patients cannot be answered completely. In this series no patients with burns of less than 40 per cent died after tannic acid therapy except one who was proven at autopsy to have an advanced septicemia. The case of O. B. is shown graphically in Chart 2. Death came at the culmination of a marked rise in the bilirubin level, and this could well have been a liver death. On the other hand, patients with other types of biliary disease often survive a much more marked rise in bilirubin.

A significant aspect of our experience, however, has been the fact that since abandoning tannic acid, no patients have survived burns of over 40 per cent of the body surface, and only two have survived burns of 35 per cent or over. It seems likely, therefore, that while tannic acid may increase liver damage when used in the local treatment of extensive burns, its use has not been attended by greater mortality.

CONCLUSIONS

Tannic acid impairs liver function following burns.

Other tanning methods impair liver function also, but to a lesser extent.

Impairment of liver function occurs also in patients treated with petrolatum gauze and pressure dressings, but it is usually mild.

The abandonment of the use of tannic acid in the local treatment of burns has not resulted in a decrease in mortality, in the series of cases presented. It, therefore, seems unlikely that the increase in liver damage observed when tannic acid is used is of great significance in the mortality among burn patients.

It would seem fair to conclude, therefore, that hepatic damage is probably not the primary cause of death in burn toxemia.

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STUDIES ON THE TOXEMIA SYNDROME AFTER BURNS

II CENTRAL NERVOUS SYSTEM CHANGES AS A CAUSE OF DEATH

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IN THE COURSE of a clinical study of burn toxemia in 1943 and 1944 six patients were observed to die of sudden respiratory arrest at a time when hepatic and renal manifestations of burn toxemia were subsiding. During the period of toxemia these patients showed varying degrees of disorientation and drowsiness leading into stupor. Occasional patients became maniacal or were subject to hallucinations, and all showed myoclonus and increased resistance to passive motion. Autopsy in every case substantiated the impression that there were organic changes in the brain and especially in the cortex and hypothalamus.

Since methods of treating burn shock have improved, a number of severely burned patients survive the first 48 hours only to succumb during the next few days to, what Wilson, and his collaborators¹ have termed "toxemia." There is a greater or lesser degree of renal damage as evidenced by oliguria and azotemia, as well as some hepatic injury.

In our experience there was associated with the evidences of visceral damage a definite degree of central nervous system involvement. The patients showed varying degrees of disorientation and drowsiness leading into stupor. All patients showed muscular twitching. The signs persisted for several days and then cleared along with the other signs of toxemia, if the patient recovered. In the fatal cases death was often sudden. Signs of renal and hepatic damage had begun to lessen and the patients had begun to improve clinically, only to suddenly stop breathing without prior warning. Some severely burned patients showed Cheyne-Stokes respirations or irregular periods of apnea prior to sudden failure. We believe these deaths were due to damage to the central nervous system, with failure of the medullary centers as a result of compression, edema and cellular lesions.

The literature contains a few reports of central nervous system damage following severe burns. Kruse² reported the case of a 14-months-old child with extensive second degree burns who developed temporary blindness, hydrocephalus and mental deterioration. Globus and Bender³ reported the case of an eight-year-old boy who developed signs of a degenerative encephalopathy secondary to extensive third degree burns. Another case

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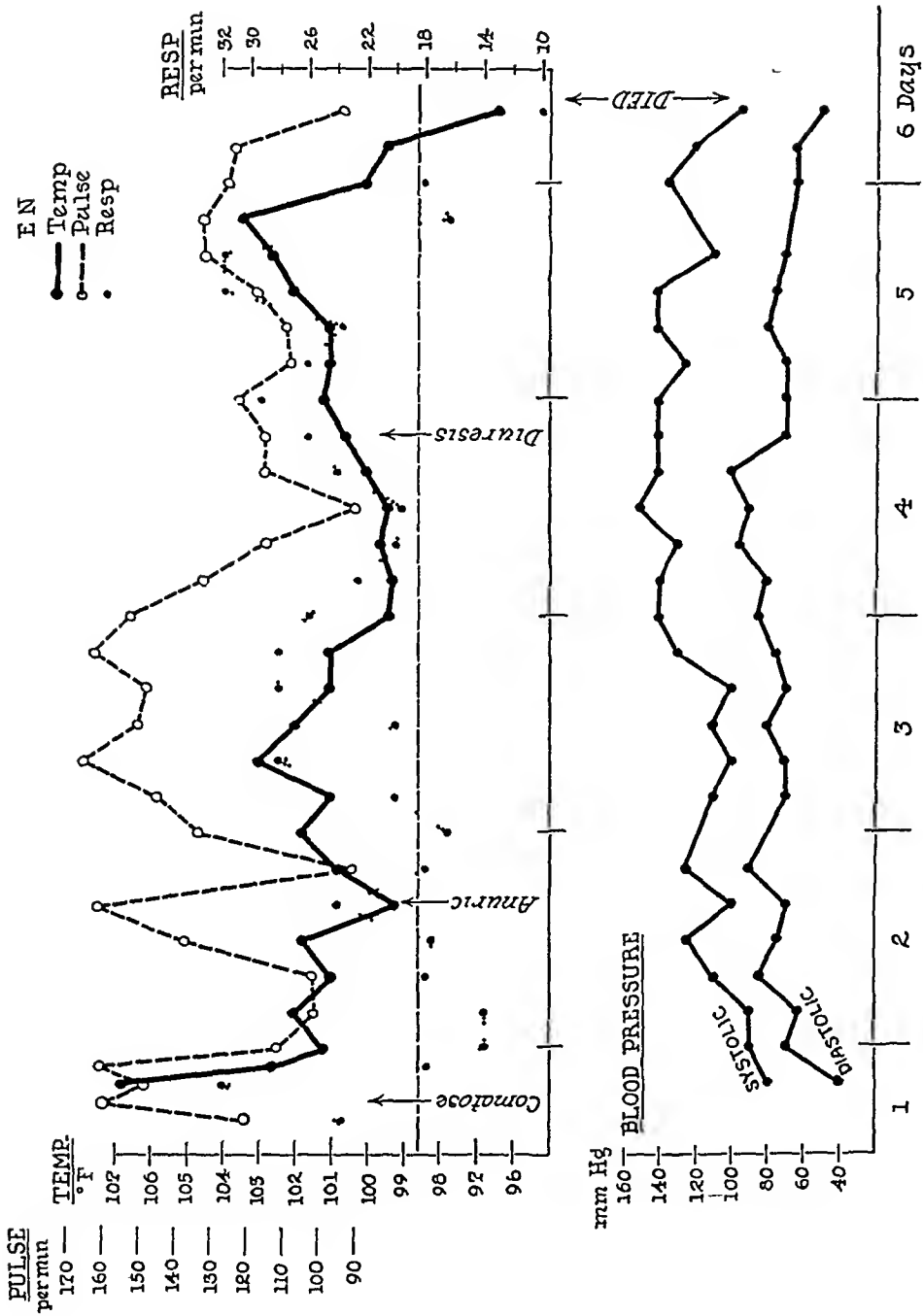


FIG 1

was reported by Roth⁴ of an eight-year-old Italian girl who developed aphasia, atetosis and mental deterioration about one week after receiving a 30 per cent scald. The changes were persisting at the time of the report. Cobb and Lindeman⁵ reported a case of severe basal ganglion cell degeneration following one of the Coconut Grove disaster cases. They ascribed the changes to prolonged anoxia. Reihl¹³ reported cerebral edema in nine cases. Christophe¹⁴ reported degenerative changes in the thalamus of dogs after cross transfusion experiments.

There are very meager reports on the pathologic changes in the central nervous system in the literature. Wilson,⁶ in reporting on a series of extensive scalds and burns, mentioned "toxic damage" in occasional cases but did not localize the lesions. Pack,⁷ in his review of the pathology of

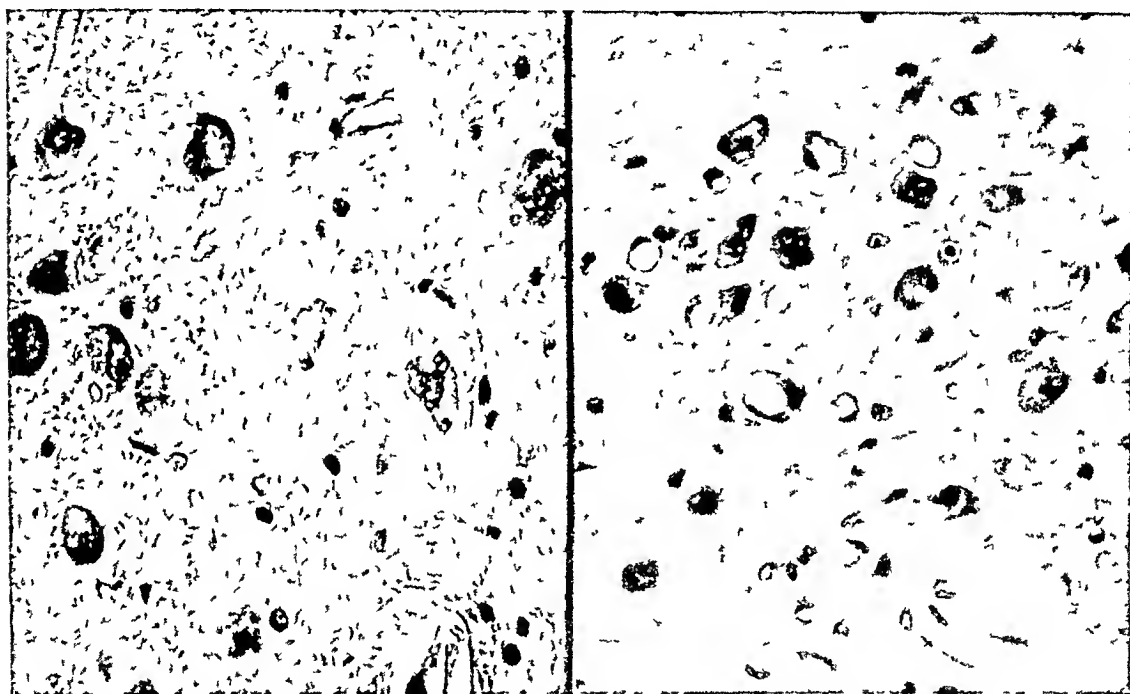


FIG 2

FIG 3

FIG 2—E N Medulla ($\times 700$ H and E stain). There is moderate edema as evidenced by the dilated pericellular and perivascular spaces. The ganglion cells are swollen, nuclei are eccentric, and some are undergoing lysis.

FIG 3—E N Hypothalamus ($\times 700$ H and E stain). This is the most severely damaged portion of the brain. The edema is marked. Ganglion cells are markedly altered, nuclei are displaced, shrunken and often pyknotic.

burns, quoted Crile as saying that central nervous system damage was seen only as the result of profound shock. Bancroft,⁸ in a review article, stated that changes in the central nervous system were not noted and Mallory and Brickley⁹ reported cortical ganglion cell degeneration in one of the Coconut Grove cases.

In 1943 and 1944 six of the severe burns seen by us in the city of Philadelphia died showing signs of central nervous system damage, and organic changes were found in the brain at postmortem examination.

CASE REPORTS

Case 1—E C, a ten-year-old white boy, was admitted half an hour after receiving a 45 per cent third degree flame burn of the upper part of the body. He

was conscious, rational, and his hands and feet were just beginning to get cold. His pulse ranged between 120 and 140 (Fig 1). Administration of plasma was started promptly, the burned areas were superficially debrided and pressure dressings of vaselined gauze applied. About three hours after being burned the child became irrational and shortly thereafter lapsed into coma from which he never aroused. Blood pressure, measured by a leg cuff, was 90/40 at this time, and the administration of plasma was continued. The hematocrit reading did not rise above 50 per cent. About seven hours after the burn the patient's blood pressure was 100/50 and the pulse ranged around 130. The hematocrit reading was 40 per cent, and the following morning, 17 hours after the burn, was 33 per cent. Urinary output was greatly reduced for two days and then began to improve. He had a number of attacks of generalized myoclonus and exhibited spasticity. On the fourth day the patient's general condition seemed much better, except for the fact that he remained deeply

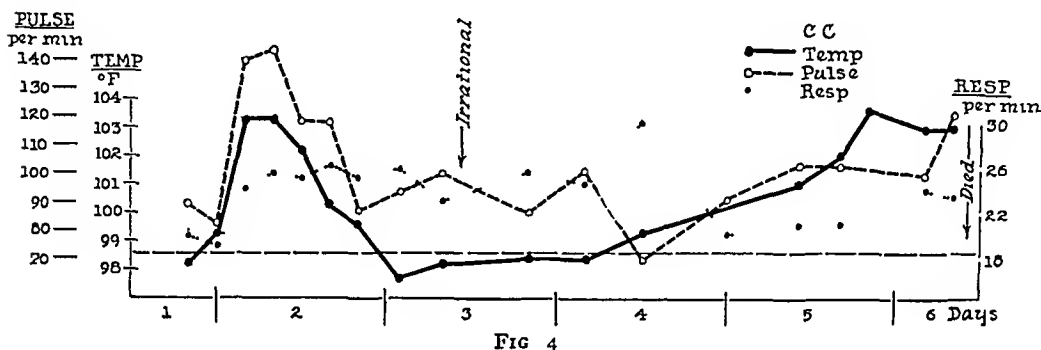


FIG 4

comatose. His temperature, which had ranged above 103° F rectally during the first 24 hours, was normal, as was his pulse, blood pressure and respiratory rate. On the morning of the fifth day his respirations suddenly ceased, and although the heart action continued for a few minutes longer, attempts at resuscitation were unsuccessful. A postmortem examination revealed severe cerebral edema with depression of the cerebellar tonsils and widespread toxic changes of ganglion cells of cortex, basal ganglia and particularly the hypothalamus (Figs 2 and 3).

Case 2—C C, a 44-year-old white male, received a 45 per cent flame burn. Burned areas were tanned with gentian violet and intravenous plasma was started. At no time was it possible to get blood pressure readings because of the extent of the burns. The patient was conscious on admission and remained so for the first few days. His pulse rose to 140 six hours after admission but later came down to 120 (Fig 4). His hematocrit reading was 65 per cent seven hours after being burned but dropped to 45 per cent ten hours after the burn and after the administration of plasma. In addition to parenteral fluids, the patient was given three liters of one-sixth molar sodium lactate orally during the second and third days. In spite of adequate fluid intake and electrolyte balance the urinary output dropped to a very low level. The patient remained markedly toxic and became confused and maniacal on the second day and stuporous on the third day. Respirations suddenly failed on the fourth day. The postmortem examination revealed extensive toxic nephrosis, and again cerebral edema and ganglion cell degeneration was widespread being most marked in the hypothalamus (Figs 5 and 6).

Case 3—V Y, a 42-year-old Armenian housewife, received a 55 per cent flame burn. She was brought to the hospital 15 minutes after the accident and intravenous plasma was started promptly. The burned areas were dressed at once with vaselined gauze and pressure dressings after very superficial debridement. The patient was conscious and oriented on admission. It was impossible to take blood pressure readings because of the extent of the burns, but the progression of the stage of primary shock

can be followed in the temperature, pulse and respiratory rate as noted on Figure 7. The hematocrit reading was 47 per cent two hours after the burn occurred and never rose above 55 per cent. It was 33 per cent after 15 hours. Parenteral fluid and plasma were continued and, in addition, the patient was given three to five liters



FIG 5

FIG 5—C C Hypothalamus ($\times 700$ H and E stain) Edema has disrupted the tissues. Ganglion cells have been damaged, as evidenced by their loss of nuclei and homogeneity of staining characteristics.



FIG 6

FIG 6—C C Cortex ($\times 700$ cresyl violet stain) Edema of tissues can be seen. Ganglion cells are swollen, nuclei are eccentric, Nissl substance disappearing. Some nuclei are pyknotic, others swollen and their identity almost lost.

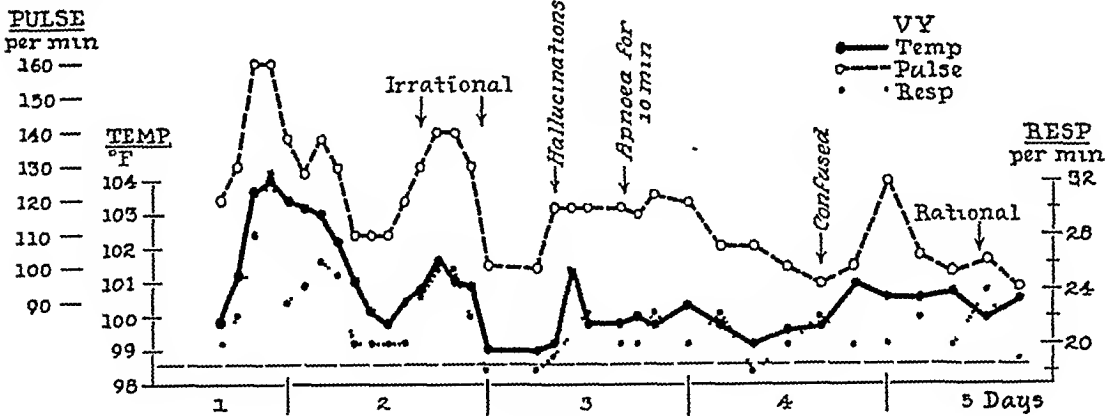


FIG 7

of one-sixth molar sodium lactate orally for the first seven days, and the urinary output remained in excess of one liter a day. On the evening of the first day, about 12 hours after being burned, the patient became disoriented and was subject to hallucinations. Twenty hours after the burn she suffered an occlusion of the right deep femoral vein, with accompanying severe arteriospasm, which endangered the leg for a number of days. On two occasions during the next two days respirations ceased for three- and ten-minute periods, during which artificial respiration was necessary. After these short periods respirations again continued spontaneously. The patient's general condition improved on the fourth day and her mental state returned to normal. She

required repeated blood and plasma transfusions with high protein feedings, and had two episodes of severe hemorrhage from extensive superficial ulceration of the rectum about the fortieth day. She died suddenly on the sixty-second day, with a massive pulmonary embolus. Postmortem examination showed that she had had several previous smaller pulmonary emboli which had given no clinical signs and a primary thrombosis of the left renal vein. Examination of the brain showed toxic ganglion cell changes affecting particularly the smaller cortical cells and the hypothalamus. There was, however, no evidence of recent brain damage, although this patient died

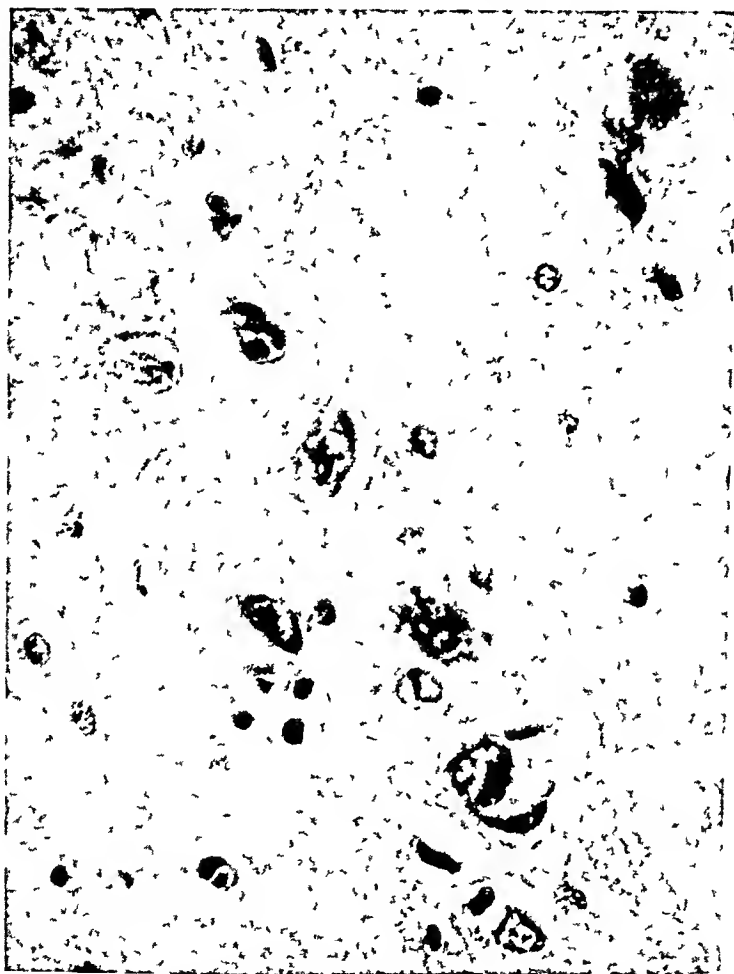


FIG 8—V V Hypothalamus ($\times 700$ H and E stain) There is little edema. The ganglion cells are swollen, however, nuclei displaced, and Nissl substance collected at the periphery of the cells. In several of the cells nuclei too are swollen and have lost their clear cut staining characteristics.

of pulmonary emboli and was undoubtedly suffering from anoxia some hours before death (Fig 8). Cerebral edema and evidences of increased intracranial pressure were not marked.

Case 4—A S., a 72-year-old white woman, previously in good health, received a 35 per cent flame burn of the head, arms and upper part of the body. She was brought to the hospital one hour after being burned and was conscious and rational at that time. The burned areas were dressed with boric acid ointment and intravenous plasma was started. Blood pressure readings could not be taken, but the pulse rate did not go above 140, and the hematocrit readings did not rise above 50 per cent (Fig 9). In addition to parenteral fluids the patient was given 3 liters of one sixth molar

TOXEMIA AFTER BURNS

sodium lactate orally daily for the first two days Urinary output remained at approximately one liter per 24 hours through her clinical course This patient showed a rise in the van den Bergh test to 27 mg per 100 o ml during the first two days This began to fall, as did the plasma nonprotein nitrogen level On the third day the patient became disoriented and semistuporous, and, began to show occasional myoclonus On the fifth day respirations suddenly ceased The postmortem examination showed fatty infiltration of the liver and a moderately severe toxic nephrosis

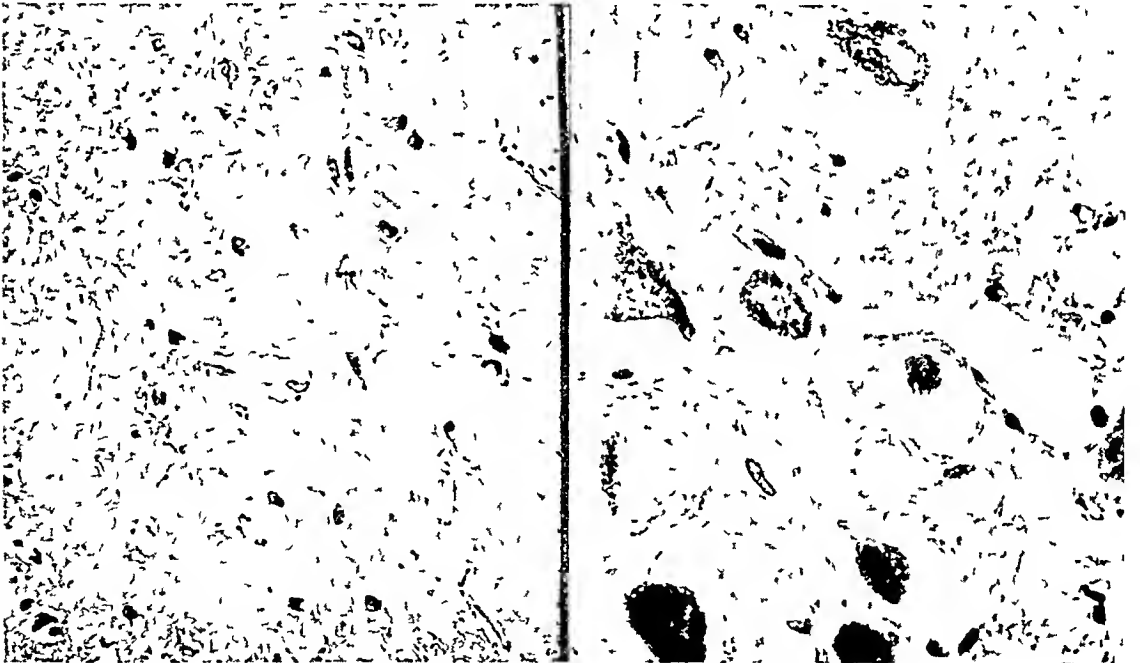
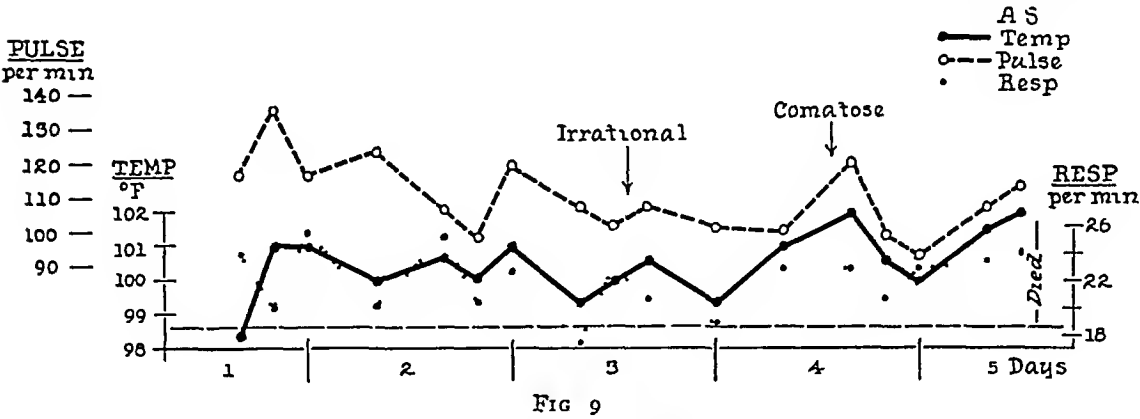


FIG 10—A S Substantia Nigra (×180 H and E stain) This low power section demonstrates principally the extensive edema, which was present throughout the brain

FIG 11—A S Substantia Nigra (×700 H and E stain) Again demonstrating the severe edema and ganglion cell changes

The brain showed severe edema with pressure on the medulla by the cerebellar tonsils, and there was widespread ganglion cell disease, most marked in the hippocampus, hypothalamus and substantia nigra Degenerative changes were noted in the walls of the smaller vessels (Figs 10, 11, 12 and 13)

Case 5—D Q, a 43-year-old white male, suffered a 40 per cent flame burn of the upper part of the body, head and arms He was admitted to the hospital 30 minutes after being burned and was conscious and rational at that time Intravenous plasma was started and the burned areas were dressed with vaselined gauze and pressure dressings His blood pressure did not fall below 100/50, and his pulse ranged between

140 and 110 (Fig 14) The hematocrit reading six hours after the burn was 65 per cent but this was 45 per cent by the twelfth hour Eighteen hours after being burned the patient passed into a state of confusion and mania His urinary output was 800 cc daily On the third day he seemed somewhat improved and was conversing with the physician in charge when in the middle of a sentence he suddenly stopped breathing Heart action continued irregularly for a few minutes longer but the patient could not be resuscitated Postmortem examination showed only moderately severe renal damage, but in the brain there was found severe edema with a pressure cone

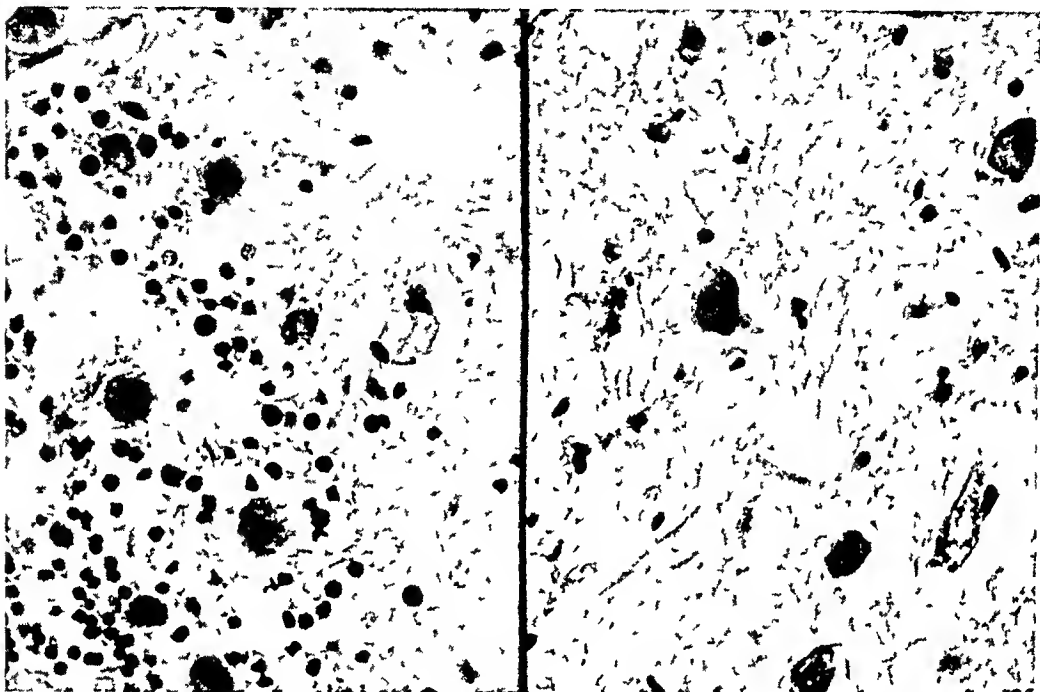


FIG 12

FIG 13

FIG 12—A S Cerebellum ($\times 700$ H and E stain) This in detail shows the changes in the Purkinje cells Vacuolization of the cytoplasm can clearly be seen

FIG 13—A S Hypothalamus ($\times 700$ H and E stain) Edema and ganglion cell changes are clearly shown

about the medulla The edema was evident microscopically and there were many degenerative changes noted in the walls of the small vessels There was widespread ganglion cell disease and again this was most marked in the hypothalamus (Fig 15)

Case 6—M C, a 28-year-old colored woman, sustained a 35 per cent flame burn of the body, and was brought to the hospital 20 minutes after the accident Intravenous plasma was started and after superficial debridement the wounds were dressed with vaselined gauze and pressure dressings The patient was conscious and did not exhibit a very marked degree of shock Her blood pressure could not be taken because of arm burns, but her pulse dropped below 120 after eight hours She exhibited fairly marked toxemia during the second and third days with a temperature of 101° to 105° F (Fig 16) However, her circulation was well maintained throughout this period She was somewhat stuporous and exhibited occasional myoclonus on the third and fourth days Respirations suddenly ceased on the fourth day Postmortem examination revealed marked cerebral edema with herniation of the cerebellar tonsils and microscopic evidence of diffuse toxic ganglion cell damage, most marked in the hypothalamus (Fig 17)

For comparison with the sections from the burned patients a section from the hypothalamus of a relatively normal brain is shown (Fig 18)

DISCUSSION —We have presented six cases of patients with severe burns who were apparently emerging from the stage of "toxemia" only to die suddenly in respiratory failure. All patients showed essentially the same signs clinically—disorientation and mania or stupor, with abrupt failure of respirations, without obstruction of the airway. Five of these patients died around

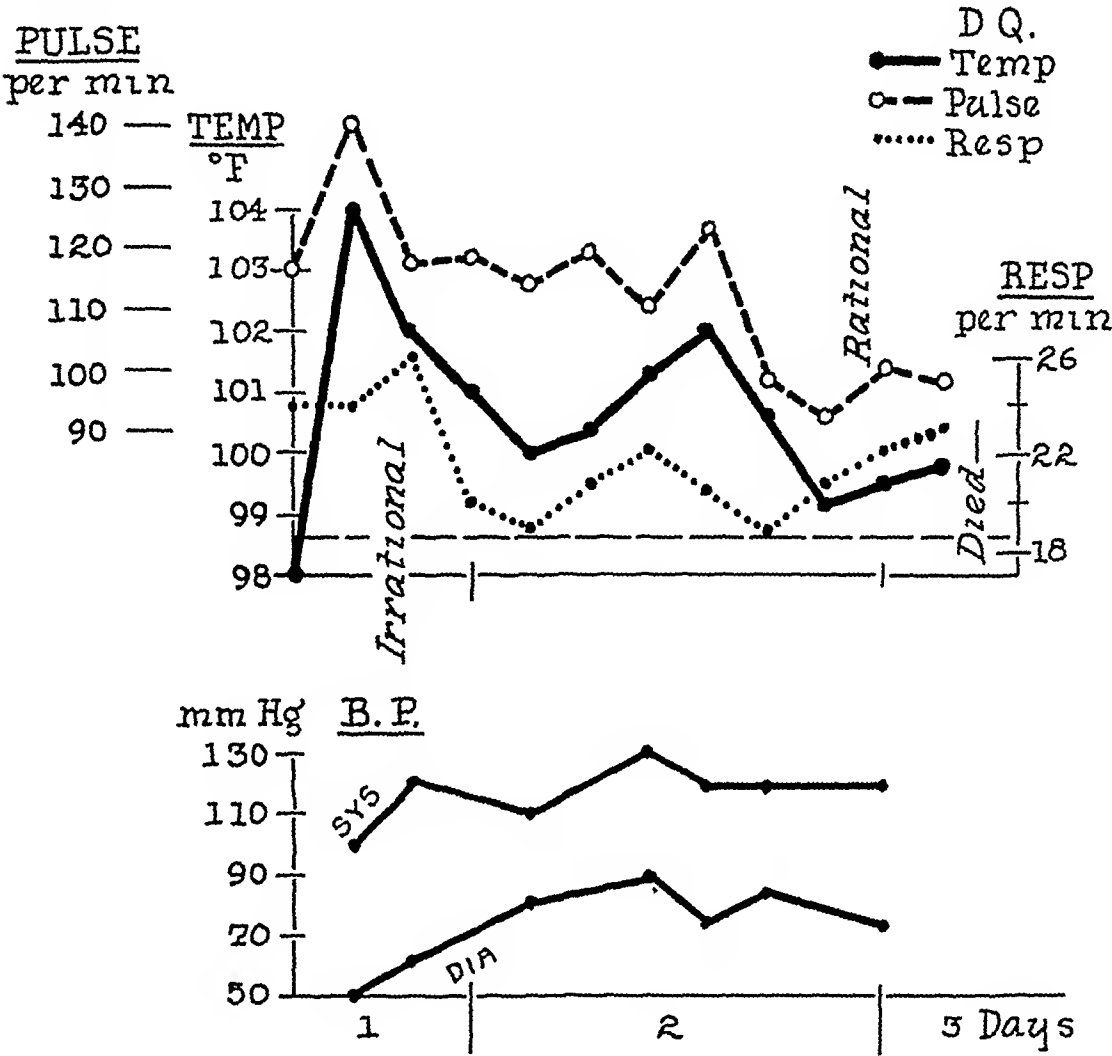


FIG 14

the fourth day after being burned. The sixth patient, with a very severe burn, showed evidence of respiratory embarrassment at this stage but survived to die later of a pulmonary embolus. This patient showed evidence of a lesser degree of toxic cell changes in the brain than other patients and there was little or no evidence of increased intracranial pressure or medullary compression.

In all of the patients dying of sudden respiratory failure postmortem examination consistently showed severe cerebral edema with evidence of marked increased intracranial pressure, including widening of gyri, narrowing of sulci, herniation of the temporal uncus through the incisura of the tentorium and herniation of the cerebellar tonsils into the foramen magnum. Microscopically, edema was revealed by widespread dilatation of pericellular

and perivascular spaces and even wide separation of the tissue itself by increased interstitial fluid. There were marked changes in the smaller vessels consisting of degenerative changes of the endothelial lining, with occasional breaks and perivascular petechial extravasations.

The ganglion cells throughout the brain showed toxic degeneration, but the most striking changes were in the cortex and hypothalamus. Of the two, the latter was the more severely involved. The ganglionic cells showed swelling and disappearance of the Nissl substance. The nuclei were

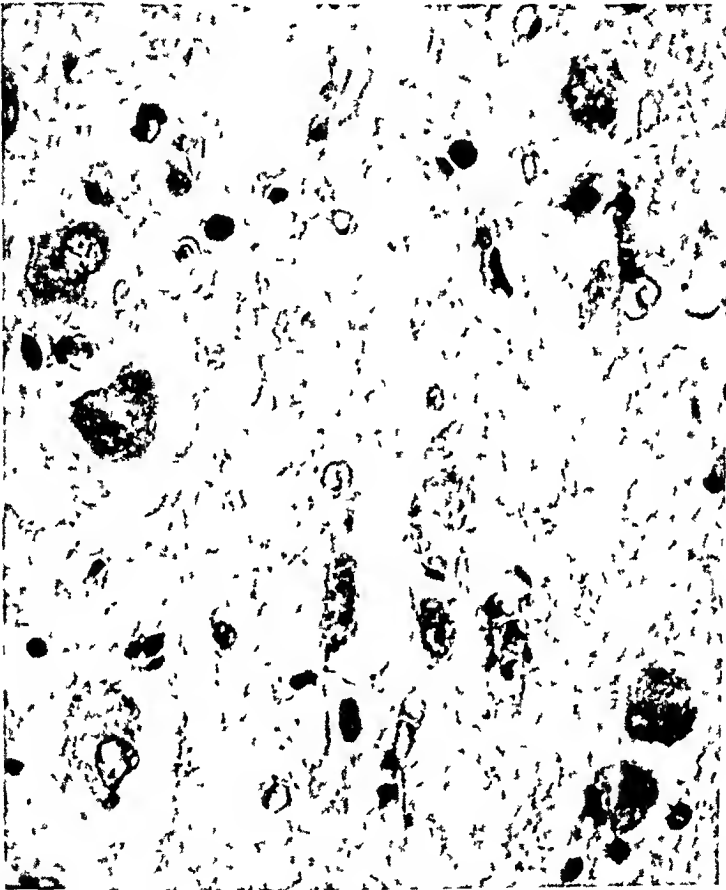


FIG 15—D Q Hypothalamus ($\times 700$ H and E stain). Edema is marked. Swelling of ganglion cells with loss of Nissl substance is demonstrated. Nuclei are eccentric, nucleoli are absent. Beginning disintegration of some cells can be seen.

usually eccentric and occasionally absent. They were often swollen and were in all stages of disintegration. In some cells the entire nucleus had become pyknotic. The cytoplasm stained palely and occasionally contained vacuoles. Many shadow cells were present. Basal ganglia and brain stem nuclei showed relatively less involvement, though definite changes were generally present (Figs 2, 9 and 10). These cellular changes varied in severity from case to case, being most severe in A S, C C, and E N. The changes were least severe in V Y, who died 62 days after her burn, of a pulmonary embolus.

The reason for these changes are not known. One explanation might be temporary anoxia as the result of shock, but in certain cases the shock was minimal and the circulation was apparently adequate, without undue hemoconcentration. Nevertheless, evidences of cerebral involvement appeared later. Patient V Y, dying of multiple pulmonary emboli, was somewhat anoxic for several hours before death, yet the brain showed no recent changes as compared with other cases. Some investigators have suggested that the visceral pathology seen in burns is due to hemoconcentration, with the formation of small thrombi and small infarcts^{10, 11}. We have examined the viscera

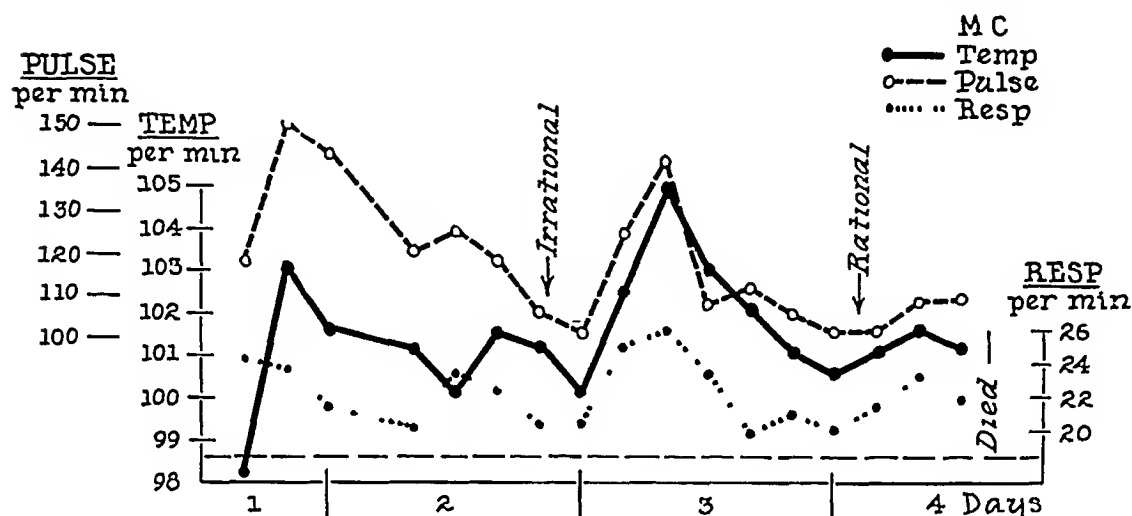


FIG 16

quite thoroughly in all these cases that died in the period of toxemia and have been unable to find evidence of such a thrombotic or embolic process, even on a microscopic scale. A third possible explanation is the circulation of some agent or toxin which damages tissue, increasing vascular permeability, and so allowing the formation of generalized edema, which is seen throughout all the organs of a patient dying in the phase of toxemia. Not only is there edema but also actual cellular destruction in the kidney tubules, hepatic radicles and the cortical cells of the adrenals. These changes have been described by us elsewhere¹².

We believe that brain damage and edema are important factors in the sudden deaths occurring during the toxemia phase of burns. Liver damage is not marked and evidence of renal damage is often subsiding when the patient suddenly dies in respiratory failure, without pulmonary pathology or preexisting cyanosis. This is similar in many ways to the death following other more obvious types of brain injury.

SUMMARY AND CONCLUSION

The case histories of six patients having severe burns and clinical evidence of central nervous system damage are presented. Five of these patients died in sudden respiratory failure when the renal and hepatic damage associated with burn toxemia was decreasing in severity. The sixth patient had two episodes of apnea during the toxic period but survived.

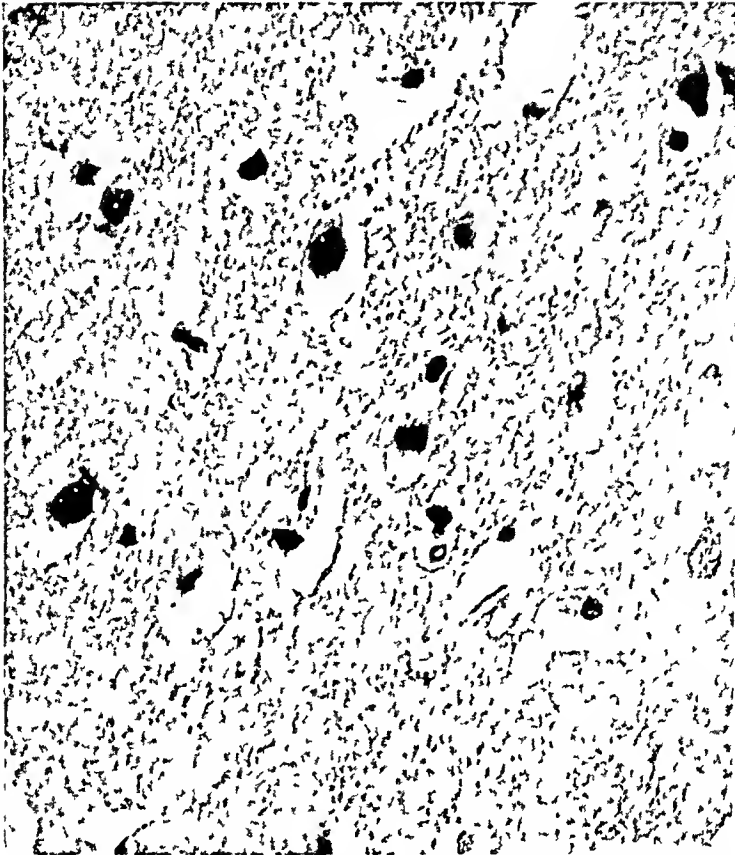


FIG 17—M. C. Hypothalamus ($\times 700$ H and E stain) Edema is present. Ganglion cells have lost much of their cytoplasm and nuclear details are disappearing.

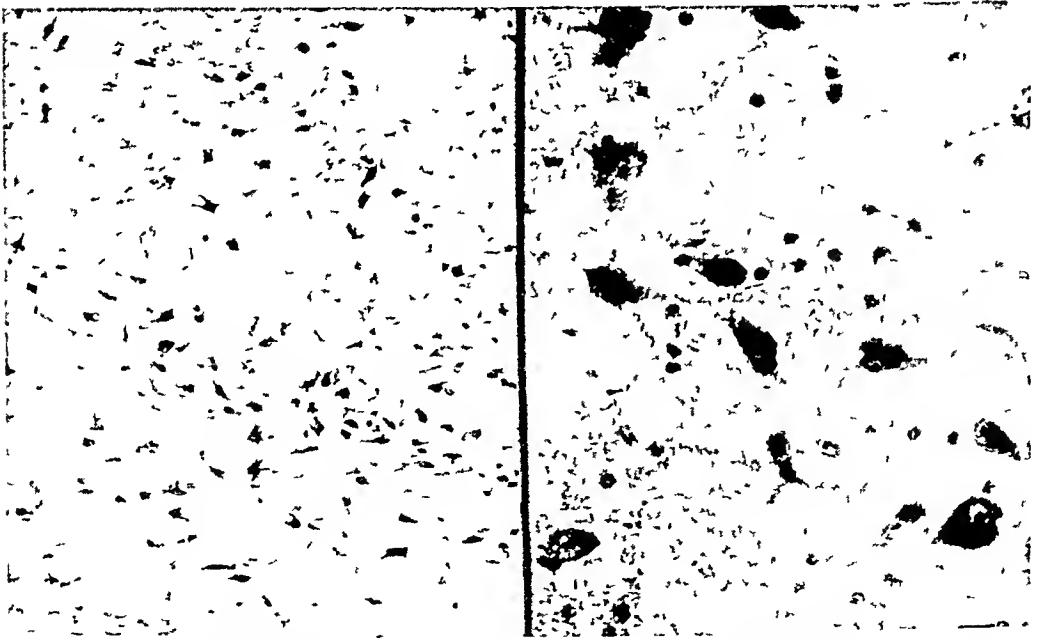


FIG 18 (A)

FIG 18 (B)

FIG 18 (A)—Normal Hypothalamus ($\times 180$ cresyl violet stain). There is no edema. Ganglion cells are not swollen, nuclei are centrally located and have well marked nucleoli.

FIG 18 (B)—Normal Hypothalamus ($\times 700$ cresyl violet stain). Same as (A).

to die 62 days later of a pulmonary embolus. The brain in this case showed evidence of damage of the same type but of lesser degree than was seen in the other five patients.

Gross examination of the brains revealed evidence of increased intracranial pressure with herniation of the cerebellar tonsils through the foramen magnum compressing the medulla.

Photomicrographs of these cases are appended showing severe interstitial edema and ganglion cell changes which were found to be most marked in the hypothalamus.

It is suggested that the central nervous system changes are an important factor in the explanation of the sudden deaths occurring in the toxemic phase of burns.

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THE PROBLEM OF THROMBOPHLEBITIS*

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HISTORICALLY, thrombophlebitis is a relatively new disease, although it probably is as old as mankind. Paulus of Aegina, about 660 A D, opened the saphenous vein, removed a thrombus and then ligated it. The use of the term phlebitis is more recent and seems to have been applied first by Breschet, in 1818. John Hunter recognized the septic form which often followed venesection. Henry Lee, in 1865, ligated the superficial veins for septic thrombophlebitis, with apparent cure. Gluck, in 1896, reported a postabortive phlebitis of the long saphenous vein cured by ligation of the common femoral. In recent years there has been a renewed interest in the subject and, as understanding has increased, treatment has improved. To adequately cope with the problem, however, further study is necessary.

CLASSIFICATION AND ETIOLOGY

(1) *Phlebothrombosis* This term is frequently used interchangeably with, and applied to, the milder types of thrombophlebitis. It indicates a thrombus within the lumen, without inflammation of the vein wall. Except following trauma, there is evidence that this does not occur. If this is true, the term should be applied only to the process which takes place in veins in various types of injury, as incised, lacerated and abraded wounds. This would be logical, more accurate and less confusing.

(2) *Thrombophlebitis* This term is applied to all types of inflammation of the vein and may be mild to severe. Thrombus formation is a concomitant manifestation of the disease and is responsible for the complication of embolism, so often fatal. Curveilher, in 1834, expounded the view that inflammation of the vein wall was the precursor of the thrombus. Later he was contradicted by Virchow, who believed that the thrombus was the primary condition and inflammation secondary. His view prevailed for many years. The concept of Curveilher, however, is generally accepted today.

In general, the disease presents three groups:

(I) *Mild or Aseptic* The localized type occurring spontaneously in varicose and normal veins. It may be well masked by the absence of clinical signs. The causes are unknown but at times it develops following strenuous activity, firm massage to the legs, and without any demonstrable reason.

(II) *Moderate* This group often complicates the various forms of surgical trauma, the puerperium, systemic infections, such as pneumonia and typhoid fever, and the xanthemata. It has been termed aseptic and toxic phlebitis. It has the characteristics of infection but cultures of the vein usually result in no bacterial growth.

(III) *Septic and Purulent Phlebitis* Bacteria are present in the vein wall and thrombus thereby accounting for the migration and metastases. Since the

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advent of asepsis, early surgery and chemotherapy, this group is seen less frequently. Outstanding examples are purulent phlebitis of the lateral sigmoid sinus in middle ear disease, involvement of the cavernous sinus in carbuncles of the upper lip and nose, pyelophlebitis and infections of the extremities.

Except at the extremes, there is no sharp line of demarcation between the first two groups and no exact information as to the etiology. Multifarious factors are responsible, as in any inflammatory process. Local resistance, generally and locally, no doubt plays an important rôle. The left leg is involved more often than the right, in proportion of 3:1. Females more often than males, in the same proportion. Selectivity of certain bacteria for the vein wall and contiguous lymphatics might be the most important factor. This phenomena manifests itself in other diseases and one may assume it might in phlebitis. Much work has been done to determine whether allergy plays a rôle.² It is difficult to understand how this could affect a structure such as vein wall and its lymphatics, without giving evidence of its effects elsewhere. This is a problem for further study.

PATHOLOGY

The literature is replete with discussions on the formation of the various types of thrombi—friable red, or adherent white, or their combinations. But there is little about the changes in the vein wall. It is only by careful study by an interested pathologist that the slight changes in the milder forms can be discerned. The vein wall may show principally a fibrosis. A diffuse infiltration of chronic inflammatory cells throughout the wall is present, mainly around the vasa vasorum. These small vessels show evidence of inflammation in the form of swollen epithelium and slight necrosis of the wall in the larger ones. There may be a diffuse inflammatory exudate throughout. Thrombotic material within the lumen may be present.

Why does a thrombus form? Tannenberg² states that leukocytic infiltration of a vein wall, or slight phlebitis, should not be regarded as very significant for the pathogenesis of thrombus. But when the inflammatory reaction is unable to bind its products, then a thrombus usually occurs. He concludes that it forms where there is morphologically recognizable necrosis or breakdown of tissue which cannot be confined or neutralized.

The pathologic physiology of thrombus formation is based upon the physiology of blood clotting. This complex process is as yet incompletely understood, and a discussion of it is not a part of this report. Suffice it to say that all factors are necessarily present when a thrombus forms within a vein. Slowing of the blood stream is thought to be a factor. This, I believe, is problematical. More likely slowing of the venous flow promotes propagation of the thrombus, rather than a causative factor. Although, in combination with other causes, it may be contributory.

Edema of varied degrees is a manifestation of thrombophlebitis. In inflammation of the vein wall there is inflammation of the contiguous lymphatics, partially or completely blocking the main channels, thereby, influencing the

degree of swelling Increased venous pressure, with resultant increase in capillary pressure, results in a tendency of fluid to accumulate in the tissue spaces Anoxemia of the local tissues further accentuates the condition It results in chronically enlarged legs, frequent ulceration, and confirmed invalidism

CLINICAL MANIFESTATIONS

The clinical manifestations show wide variation, thereby, making the diagnosis of the degree and extent of the disease difficult This is aptly illustrated in the cases cited herewith

In the mild types, the symptoms may be so slight as to pass unrecognized The patient may complain of a vague ache in the legs upon standing or prolonged activity At times there may be slight swelling There is no elevation of temperature or pulse, or other constitutional symptoms, except the patient's desire to elevate the legs, the discomfort abating with rest There may be a history of massage or a fall traumatizing them Examination usually elicits tenderness in the calf region, or at some site along the superficial veins Frequently tenderness is present on the plantar surface of the foot or the adductor group of muscles These findings are consistent with muscle fatigue, but a localized, tender area in the calf region or a firm, slightly discolored spot in the superficial veins are adequate signs to make a diagnosis of thrombophlebitis Further activity aggravates the symptoms The patient may be suddenly seized with a chest pain, with some dyspnea and at times a cough and hemoptysis The temperature and pulse rate becomes slightly elevated A roentgenogram of the chest shows fluid in the costophrenic sulcus, with lung fields relatively clear A diagnosis is made of pulmonary embolus complicating thrombophlebitis

In the moderate group the symptoms and signs are more obvious There is a history of some recent surgical intervention, or systemic infection, or the puerperium with convalescence progressing satisfactorily The eighth to fourteenth day there may be mild pain in the calf region, plantar surface of the foot or mid thigh Dorsiflexion of the foot frequently intensifies the calf pain, but may not alter it There is some edema and the temperature and pulse moderately elevated Sometimes a slight chill heralds the onset Pulmonary embolus is a probable complication in this group

The more advanced cases present greater swelling, more pain, and the temperature and pulse further elevated The leg may become markedly swollen, the skin white and mottled, and having a stretched appearance The leg is warm, but the tissue temperature is lowered There is exquisite tenderness over the entire extremity

The following three cases are reported because of the different history in each, and pulmonary embolus had occurred in two before the disease was definitely recognized

Case 1—New York Hosp No 310172 E S, female, age 40 September 17, 1942
Chief complaint sudden pain in the right lower chest beginning two days ago, severe for

the past nine hours. Some dyspnea, no cough or hemoptysis. A few small varicose veins present which had been injected. During the past year she had also received vigorous massage to the legs. One month ago, following an injection in the right leg, there was increased heaviness and swelling. For several months there has been slight edema and a general ache in both legs after prolonged activity.

Physical Examination—Diminished breath sounds in the right lower chest and a few râles. Heart normal, B P 134/78, pulse 80. Right leg. An irregular, tender cord palpable in the popliteal space extending downward to the midcalf. Small thromboses present at the site of injections. No change in color of the skin, temperature normal, no acute pain or dorsiflexion of the foot.

Laboratory Data—Roentgenograms of the chest "showed right diaphragm elevated with obliteration of the costophrenic sinus and slight mottling scattered at the extreme base." Hb 12.5 Gm, red blood cells 4,450,000, white blood cells 9,100, polymorphonuclears 79%, lymphocytes 21%. Platelets high normal in four subsequent counts. Two days later the patient coughed up dark bloody sputum, repeated the second day following. There was tenderness along the saphenous vein, right leg and calf region. Fourth day, heparin advised. Fifth day, roentgenograms of legs, "highly suggestive venous stasis much more marked in the right, probably associated with thrombosis of deep veins." There was slight edema of the legs. Ninth day, venogram right leg, "findings suggestive of thrombus of the femoral vein with probable involvement of one of the deeper branches of the popliteal vein."

Clinical Diagnosis Pulmonary embolus, with a probability of others occurring with more serious consequences. It was, therefore, decided that ligation of the saphenous and femoral veins in the right leg was indicated.

Operation—September 30, 1942. Under avertin-local anesthesia, using 1% novocaine, a four-inch slightly oblique longitudinal incision was made high in the right thigh, extending from one inch above the flexion crease downward. The saphenous vein was isolated to its junction with the femoral, and, to palpation, was free of thrombus. The femoral sheath was incised, the artery retracted laterally and the vein isolated below the profunda branch and upward, to include two inches of the common femoral. To palpation, this was free of thrombus. Ligatures were placed around the vein below the profunda branch and not tied. The vein was incised longitudinally and free bleeding followed, which was controlled by pull on the ligatures. An aspiration catheter was placed within the lumen proximally and distally, without recovery of thrombotic material. The ligatures then were tied, reinforced, and the vein divided between. Elastic bandages were placed on the leg and the patient encouraged to exercise in bed.

Seventh postoperative day. Slight edema around the ankle. She was kept in bed until the 21st day.

Twenty-fifth postoperative day. No swelling of the leg. The patient discharged the 38th day.

November 15, 1942. Six weeks later. There was some swelling of the lower leg, and there was a localized area of thrombophlebitis below the knee.

December 4, 1942. The patient had a sense of tightness in the popliteal space when ascending and descending stairs. Otherwise felt very well. Continued to be normally active and periodically continued to wear an elastic bandage. The circumference of the right calf 5.5 inches below the lower border of the patella measured 15 inches and the left 13.75 inches.

May 23, 1944. Twenty months after ligation. The patient was normally active, felt well, with no discomfort except some heaviness after long periods of standing and during the menstrual function. She had noticed no swelling of either leg. The color was normal and there was no further development of varicose veins. Six inches below the lower border of the patella the right leg measured 14.5 inches in circumference and the left, at the corresponding level, 13.75 inches.

It is of interest that the femoral vein at the site of ligation, remote from the probable site of thrombus, showed no thrombotic material but did show evidence of inflammation of the vein wall. This patient fits the clinical description of phlebothrombosis, pathologically, it is a thrombophlebitis (Fig 1) Figure 2



FIG 1—This section of femoral vein shows an outpouring of acute inflammatory cells about the vasa vasorum. There is enough infection in and about these vessels to make a diagnosis of thrombophlebitis. There is no distortion of the morphology of the walls of the vessels.

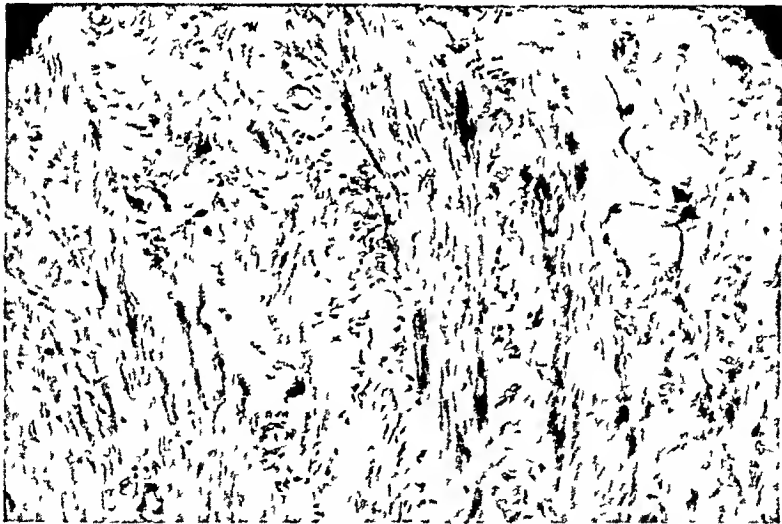


FIG 2—Saphenous vein cross section shows focal areas of inflammation within the muscularis, as evidenced by interstitial outpouring of lymphocytes. This generally is seen about the vasa vasorum. Patient has spontaneous thrombophlebitis below the knee. (Section from the femoral junction)

shows a section of the saphenous vein. This patient had a localized thrombophlebitis occurring spontaneously in the superficial system near the knee.

Case 2—New York Hosp No 253723 C M, age 53. Six weeks prior to admission to this hospital, a D and C was performed elsewhere. Changes were found suggesting malignancy and 2400 hours of radium were administered. Otherwise the history irrelevant.

Examination Normal findings B P 110/78

Laboratory Data Urine analysis—sp gr 1.015, albumin very faint trace, microscopic—few white blood cells Blood count—W B C 6,800 to 9,900, diff polymorphonuclears 76%, lymphocytes 24% Hb 12.8 Gm, R B C 4,840,000

Operation—December 14, 1942 Under avertin-gas-oxygen anesthesia, a panhysterectomy was performed through a suprapubic midline incision. On the left side of the cervix there was a slight necrosis with a small collection of mucopurulent material, which cultured *Staphylococcus aureus hemolyticus*. The appendix was removed.

The postoperative course was uneventful, the patient out of bed the 8th postoperative day. On the 10th postoperative day, there was pain in the left calf region. Examination revealed tenderness in the area, but no edema, redness or increased heat. By the end of the day the left leg was tense and warm, and the superficial veins full. The leg was elevated and a cradle, with lights, placed over it. The patient was given sulfadiazine and sodium thiosulfate. Within the next three days the pain subsided.

She continued to improve until December 29, 1942, the 15th postoperative day, when there was sudden pain in the right lower anterior chest. No abnormal findings upon examination. By 7 P.M. the pain in the chest was more severe and made worse by respiration and movement. Pleural friction rub heard in the right axillary region. Respirations 20, pulse 98, rectal temperature 37.4 C. On the 16th postoperative day, moderate retrosternal pain, patient somewhat cyanotic. Some edema of the left leg. Heparin advised. *Diagnosis* Subsiding phlebitis left leg and pulmonary infarct. W B C 10,850, polymorphonuclears 87%, lymphocytes 13%. Platelet count normal on four subsequent counts.

Nineteenth postoperative day. There is persistent chest pain on deep breathing, no pain in the calf region. Patient had been on continuous infusion of 2% heparin in normal saline for four days. Clotting time maintained at 20 minutes. (At times up to 40 minutes). A roentgenogram "showed prominent hilar markings on the right. The right diaphragm is slightly elevated and there is obliteration of the right costophrenic sulcus."

Impression Findings compatible with the clinical evidences of infarct.

Twenty-second postoperative day. Eighth day of continuous heparin. No further signs in the chest nor pain in the leg. Heparin discontinued the 10th day.

Twenty-fifth postoperative day. Patient allowed to exercise in bed, and three days later allowed out of bed. At this time there was no complaint.

Thirty-first postoperative day. Patient had another acute episode of pain in the right lower chest, which probably represents another infarct.

Thirty-second postoperative day. At about 2 A.M., was awakened by another acute pain in the right chest associated with cyanosis and labored respirations. Pulse rate increased to 110. Examination revealed diminished breath sounds over right chest. Heart rapid, B P 106/66, no mediastinal shift. Legs appear normal except for slight fullness of the lower veins. Papaverine and aminophyllin and oxygen given. Heparin started. At this point, it was noted that there was a history of venous thromboses in the father, sister and brother.

The patient continued very ill. On the 35th day, an EKG showed "the tendency toward the low amplitude of the QRS complexes and the T waves throughout suggest myocardial damage. Their form is not unlike that seen following pulmonary infarction. Heart rate rapid." The patient's temperature and pulse remained elevated, breathing became more comfortable, but the râles and friction rub persisted. Heparin discontinued the 10th day. Prothrombin 39%.

Fiftieth postoperative day. There was a slight twinge of pain in the right lower chest, but the patient was sitting up in bed for meals.

Fifty-second postoperative day. There was slight pain in the chest to the left of the

sternum with some dyspnea and moderate cyanosis. This probably represents another infarct.

Fifty-third postoperative day. Tenderness present in the left calf with slight edema. It measures 2 cm more than the right. Ligation of the femoral and saphenous veins advised. Venogram suggested, but was later countermanded.

Operation—February 11, 1943. Under avertin-local-cyclopropane anesthesia, a four-inch slightly oblique incision was made in the left upper thigh, extending from two inches above the flexion crease downward. The lymph nodes were enlarged, but not acutely inflamed. The saphenous vein was isolated to its junction with the femoral. Grossly, there was no evidence of thrombus. The femoral sheath was incised, it was moderately adherent to the vein. The artery retracted laterally and the vein isolated.



FIG 3—Femoral vein. Section shows a somewhat fibrotic wall surrounding which there is considerable thrombotic material apparently lodged in neighboring veins or possibly in the wall of the vein itself. There is a bit of thrombus which is definitely intraluminal in the main channel. Examination of the vasa vasorum shows slight evidence of inflammation in the form of swollen epithelium and slight necrosis of the wall of some of the larger vessels. There is a diffuse but scanty inflammatory exudate throughout the wall of the vein.

two inches below the profunda and upward to include the common femoral. The vein was soft, without evidence of thrombus. The superficial femoral was opened between two untied ligatures and free bleeding encountered. Aspiration was done without recovery of thrombotic material. The ligatures were then tied and the vein divided. The patient withstood the procedure well. An elastic bandage was applied and the patient encouraged to exercise in bed.

Out of bed the seventh day. At this time there was no tenderness in the calf region, but slight edema persisted. She was active, rapidly improved, and was discharged February 27, 1943, 16 postoperative days after ligation.

June 20, 1943. Four months later the left leg, 10 cm below the lower border of the patella, was 37 cm in circumference and the right 34 cm. There was no edema or tenderness. At the present time (September, 1944) the patient is normally active, but has some discomfort after undue activity or standing. There is no edema and the leg measurements are the same as they were one year ago (Figs 3, 4 and 5).

In view of the original pathology, it would have been logical to conclude that this patient had an iliofemoral thrombophlebitis, and because of this the venogram was countermanded. This case indicates that heparin evidently is of

little benefit in preventing emboli when the disease has developed. The sections of the veins illustrate the point that the disease is present remote from the probable site of the thrombus.

Case 3—New York Hosp No 220149 L B, female, age 27. Four years ago the patient was delivered of her first child. It was a normal delivery and uneventful convalescence. Otherwise history irrelevant.

On October 19, 1942, without a difficult or prolonged labor, the patient was delivered of her second child. The convalescence was smooth and satisfactory. In the 10th day she developed moderate pain in the left calf region and medial left thigh.

Physical Examination revealed slight edema about the left ankle, with some tenderness in the calf region and, superficially, four inches below the fossa ovalis. Heparin suggested, also ligation of the saphenous and femoral veins.

Operation—November 3, 1942. Under avertin-nitrous oxide anesthesia, a four-inch incision was made in the left upper thigh, extending from two inches above the flexion crease downward. The saphenous

vein isolated, and was firm, indicating the presence of a thrombus. The femoral sheath was incised and the vein freed below the profunda and upward to include the common femoral. All veins were filled with thrombus. Ligatures were placed around the common femoral and the vein incised longitudinally between them. A soft, friable thrombus presented. There was no bleeding. Using a glass catheter, thrombotic material was aspirated from the proximal segment. Because this was too short to recover all the thrombus, a No 16 F urethral catheter, with the tip cut away, was used. This was long enough to extend well up into the external iliac vein. Many pieces of friable thrombus were removed and as the final piece, about three inches long, came away there was sudden free bleeding. The ligatures were then tied and the vein divided between the ligatures. Section of the femoral vein was taken for study. The saphenous vein was not separately ligated.

The patient withstood the procedure without untoward event. Tensor elastic bandage was applied.

First postoperative day. Tenderness in the left leg had entirely disappeared, there was no increase in swelling and no elevation of temperature. The patient encouraged to exercise in bed.

Fourth postoperative day. Some tenderness present in the left calf and slight swelling about the ankle. Sutures removed on the sixth day. The incision healed by primary union.

Seventh postoperative day. Patient allowed out of bed. There was still some tenderness and swelling persisting. Measurement, 18 cm below the lower border of the patella, left leg 36.25 cm in circumference and right 33 cm. Patient was discharged from the hospital the 10th postoperative day.

She continued to be normally active and wore the elastic bandage for several months.



FIG 4.—Saphenous vein is apparently less affected than the femoral. Its endothelium is vacuolated and swollen. There is considerable hemorrhage into the wall. The vasa vasorum are very small and insignificant. They contain rather numerous leukocytes in some instances.

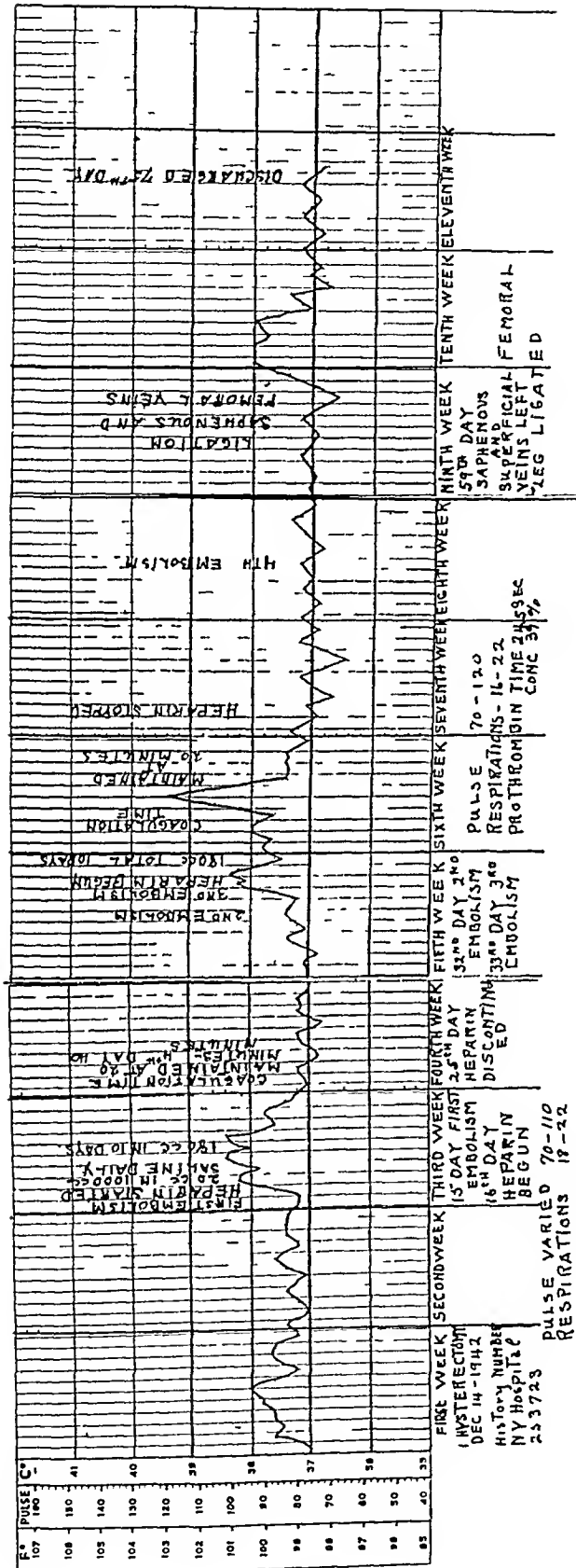


FIG. 5.—Case 2. Temperature curve showing slight elevation prior to the complaint of pain in the calf and the first embolism.



FIG 6—Femoral vein. There is rather a diffuse infiltration of chronic inflammatory cells scattered throughout its wall. This is not perivascular in nature, being found only around the vasa visorum, as in previous sections, but is present as a diffuse chronic inflammatory reaction.



FIG 7—Case 1. Infrared photograph 20 months after ligation of the superficial femoral and saphenous veins. Except for slightly more prominent superficial veins, there is practically no difference in the legs.

Eighteen months later there was no edema but the left leg was slightly larger than the right. There was some discoloration on each side of the foot. The small superficial veins were more obvious than those of the right leg. At times she complained of mild discomfort along the tibial crest after prolonged activity (Figs 6, 7, 8 and 9).

The above cases illustrate the mild to moderate types of thrombophlebitis. In each there was a different clinical history and, except for slight variation in degree, the symptoms and signs were the same. In two the complication of pulmonary embolus had occurred before the presence of the disease was fully appreciated. The third illustrates the fact that the saphenous and femoral sys-

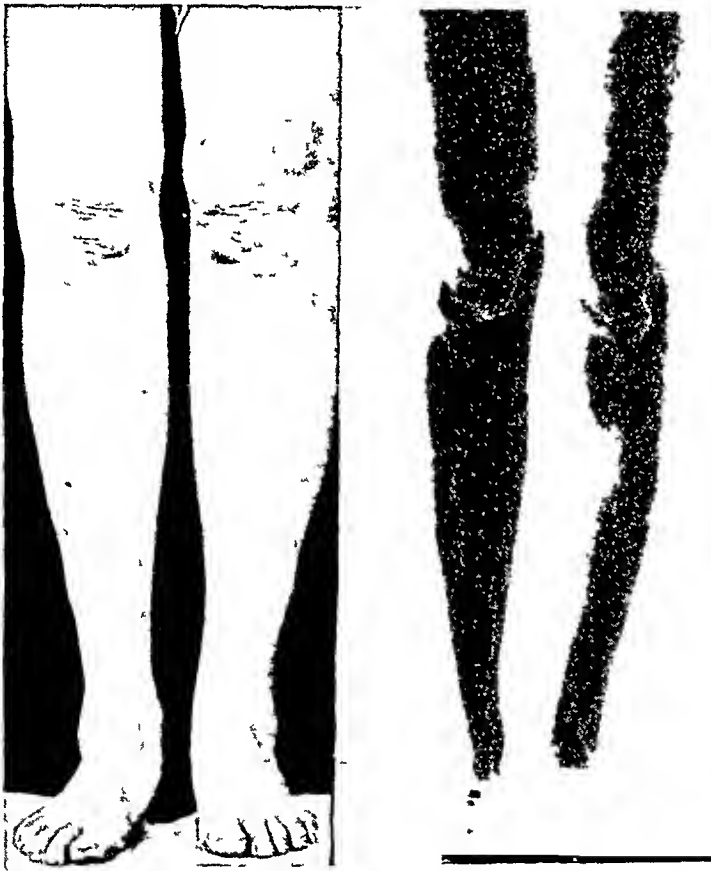


FIG 8—Case 2. Showing the legs 18 months after operation. An average photograph does not show the superficial veins as does the infra red on the right. There is little difference in the two legs.

tems can be completely occluded by a thrombus, with few signs, little pain and practically no edema. Whether the disease would have advanced further with conservative measures is problematical. It is reasonable to assume that it would have.

COMPLICATIONS AND SEQUELAE

The most serious complication is embolus in the lungs. They may be small, resulting in localized areas of pneumonitis. Larger ones produce infarcts which may go on to abscess formation. The massive ones cause sudden death. When the portal system is involved, emboli cause infarction and suppuration in the

liver In carbuncles of the upper lip and nose, the cavernous sinus may become the site of a thrombus and, in middle ear disease, the lateral sigmoid sinus is often affected The mortality rate in this group is high

Chronically enlarged legs, with lowered tissue resistance resulting in ulceration are common sequelae Inactivity frequently aggravates the swelling Frequent recurrences of thrombophlebitis, with pain and increased edema, are characteristics of the disease Prognosis for survival is good, but for complete recovery, poor Some patients appear to be relatively well for an indefinite period, then there is a recurrence, with disability

TREATMENT

Prophylactic treatment is of the utmost importance Abnormal physiology should be corrected Strict asepsis and careful manipulation of tissues during surgical trauma are important Venous stasis should be counteracted by early motion It may be that the anticoagulants will find their rightful place in the prophylaxis of the disease⁵ By study and experience, it is necessary, however, to assay heparin and dicumarol further

The entire therapy of thrombophlebitis is being reopened and reviewed The active treatment has consisted of conservative measures, which have occupied the center of the stage Complications have not been lessened by these measures Morbidity has been long and improvement slow Return to activity requires weeks to months, with enlarged legs, and chronic invalidism common residuals

In 1936, it was observed that localized thrombophlebitis, in superficial veins, rapidly abated when the large vein above the involved site was obliterated by injection Pain and the signs of inflammation disappeared, local tenderness and edema more slowly Ligation of the saphenous vein at the femoral junction was then carried out in varicose and normal veins with completely satisfactory results Healing of the disease progressed rapidly Frequently the involved vein recanalized, with persistence of the varicosities Multiple ligation



FIG 9—Case 3 Two years after ligation of the common femoral Except for slight thickening there is little difference in either leg

was then resorted to, with sometimes excision of the involved segment of vein when there was minimum reaction of the surrounding tissues. The results have been uniformly good. Eighty-six cases have been operated upon (25 during the past year), seven bilaterally, with excellent results in 84. One patient had a local recurrence about the knee two years later. This promptly subsided upon activity and wearing an elastic bandage. The second patient had immediate activation of the disease, which subsided after six weeks. This patient had a history of recurring thrombophlebitis with numerous roentgenray treatments extending over several years. All patients were permitted active motion out of bed after 24 hours, and wore an elastic support until the edema subsided. Most discarded them automatically within two to four weeks.

When the deep venous system is involved, it is even more important that ligation of the saphenous and femoral veins be carried out. The procedure minimizes complications and hastens recovery. Since 1942, 18 cases have been operated upon. There have been no complications. Pain rapidly disappears, the edema subsiding more slowly. Elastic bandages are immediately applied and the patient encouraged to exercise in bed. As soon as the reaction about the incision has subsided, the 4th to 7th day, the patient is allowed active motion out of bed. They continue to wear their elastic support until swelling has disappeared. The patient will automatically discard this after a few weeks. However, some slight swelling might persist for several months. In this group there have been no recurrences, no chronically enlarged legs and no ulcerations.

In cases of long-standing thrombophlebitis, there follows an established edema of varying degrees. Wearing of an elastic support and active motion results in some abatement of the swelling. Recurrences are common and the patient always is uncomfortable when active. The patient with chronically enlarged legs, with or without evidence of local activity of the disease, it is important to determine the patency of the venous system. This can be done by the venogram. If the veins have recanalized and an ulcer is present, ligation should be carried out. This relieves pain and promotes repair. If there is complete closure of the femoral system by fibrous tissue, operative intervention

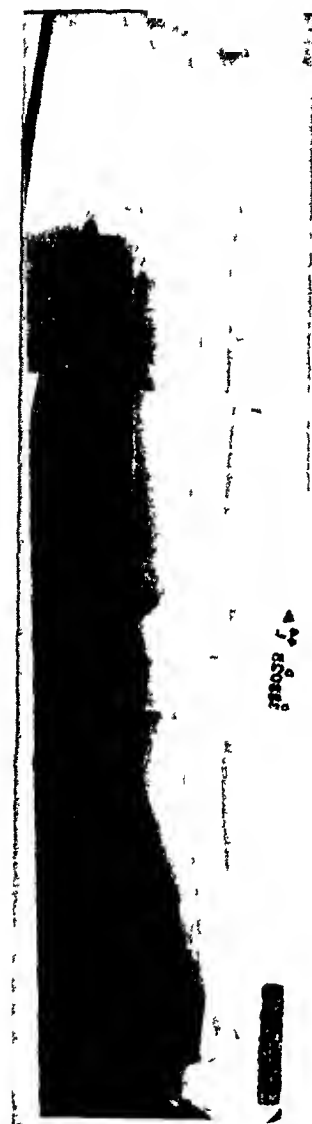


FIG 10.—Venogram of the left leg. Patient age 26. Following a pregnancy two years ago phlebitis developed in the left groin. Patient in bed nine weeks, with conservative measures. For many months wore supportive bandages. For the past year recurring attacks of phlebitis, locally, at different sites along the leg, with redness and swelling. This shows complete fibrosis of the femoral and iliac veins. Surgery of no value.

of the femoral system by fibrous tissue, operative intervention

will be of little value (Fig 10) In established edema, ligation has proven of little benefit

Reports are appearing in the literature, attesting the value of ligation in thrombophlebitis Allen, and his associates,³ recently reported a series of 202 cases with satisfactory results Buxton, *et al*,⁴ report their results in ligation in long-standing deep phlebitis Further efforts are being made by others Additional experience is necessary to fully evaluate this type of therapy, but the results to date justify its more general adoption

Surgical intervention in the suppurative group is essential, because the results with conservative measures are uniformly poor

Heparin and dicumarol may prove to be important adjuncts in the active therapy of this disease

SUMMARY AND CONCLUSIONS

(1) A review of the causes of thrombophlebitis and a simplified classification are presented

(2) An attempt has been made to clarify the pathology of the disease and the relationship of thrombus formation to it

(3) Clinical cases have been presented illustrating the vagaries of the disease, often well-masked symptoms make it difficult to determine the activity and extent of the pathologic process

(4) Complications and sequelae are discussed

(5) The treatment of the disease by prompt ligation is advocated, with results in 104 cases attesting its therapeutic value

(6) Phlebography is indicated to determine the patency of the venous system in long-standing thrombophlebitis

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WHEEL-FLUORESCENCE

A NEW METHOD OF EVALUATING PERIPHERAL VASCULAR DISEASES PRELIMINARY REPORT

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THE PURPOSE OF THIS PAPER IS to introduce a new and simple test which promises to be an accurate means of revealing certain fundamental facts of diagnostic, prognostic, and therapeutic importance in cases of peripheral vascular disease. In the authors' experience to date, this test appears to be the least time-consuming and most easily readable method of study now in use for similar purposes. Clinical correlation, comparison with other known methods, and a sound basis in logic attest to its reliability. The information obtained (1) reveals data regarding the extent and degree of vascular insufficiency, (2) apparently indicates whether the predominant difficulty is organic or vasospastic, (3) helps determine the prognosis of the studied limbs, (4) aids in deciding the therapeutic approach best suited to the individual, and (5) locates the lowest level of amputation (when necessary) which can support prompt healing.

The test consists of observing the presence or absence of fluorescence in surface scratches made fluorescent by injection of intravenous fluorescein followed by inspection under specially filtered ultraviolet light. Presentation of the important elements comprising the test follows.

SURFACE FLUORESCENCE

In 1931, Lange and Wollheim¹ demonstrated that the luminescent property of fluorescein could be observed in the body surfaces if after intravenous injection of this substance, a proper light source was used. Technical difficulties precluded immediate general adoption of this discovery, but by 1942 it had been worked out in a practical way and was presented with several recommended clinical applications.² This presentation opened a new field for clinical investigation, and since then Lange, and his coworkers,^{3, 4, 5, 6, 7} and others,^{8, 9, 10, 11} have developed many effective ways of using the technic and have established its harmlessness. Credit is due these men for the discovery and development of a widely applicable clinical tool.

One of the applications of the technic set forth by Lange and Boyd was its use as a test for peripheral vascular disease. When so employed, skin fluorescence was said to be delayed, less intense, or absent where reduced vascularity existed. On the basis of this report, the procedure was adopted at the Wisconsin General Hospital as a comparative method in a general study of the various tests for peripheral vascular disease. The results obtained were disappointing. Fluorescence regularly appeared wherever

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vascular flow of a degree sufficient to prevent complete infarction existed. The delay in appearance of fluorescence, which was said to occur in areas of reduced vascularity, was never observed with certainty, and the intensity was affected by so many extraneous factors that it could not be accurately evaluated. In areas of dermatitis or pigmentation, fluorescence was reduced, spotty, or absent, in areas of inflammation and/or infection, it was promptly and brilliantly apparent, regardless of obviously reduced circulation, and even where the skin was not visibly disturbed, local vasomotor effects or unknown factors caused a marked variation in intensity. Furthermore, foreign materials such as boric crystals, vaseline, and common antiseptics produced interfering fluorescence of their own and at times could not be adequately removed in important areas. Lange freely admits many of these difficulties and states that careful judgment in reading the test is a primary requisite. In his hands, results have been better, but the care and experience necessary to properly interpret the test seem to us to hamper its effectiveness as a generally acceptable procedure. For these reasons, it was about to be discarded when the discovery was made that employment of skin fluorescence as a method of measuring the fundamental skin response to injury resulted in a simple, practical, and effective test.

SKIN REACTION TO INJURY AND ITS SIGNIFICANCE

It is a matter of fundamental knowledge that the skin responds to injury by the production of a reaction which has as its purpose the ultimate repair of the injury. The degree of reaction is dependent on the extent of trauma and the ability of the tissue to respond.

Normally, the skin reacts to a simple scratch, pinprick, or the introduction of histamine with a triple response.¹² The difference in reaction to these various agents is quantitative only. The first element is the "red" reaction which appears quickly at the exact point of injury. This reaction appears regardless of nerve supply or blood flow, and is due to a local active vasodilatation of the terminal arterioles, venules, and capillaries of the skin. The second element is the so-called "flare" which irregularly surrounds the point of injury as a pink halo. This phenomenon represents an axon reflex causing vasodilatation in the slightly larger well muscled group of arterioles in the skin, and depends for its occurrence on both an intact local nerve supply and relatively normal blood flow. In the absence of either or both of these factors it does not appear. The third element is the appearance of a "wheal." This part of the reaction is due to an alteration in permeability of the vessel walls and never occurs unless adequate blood flow is present. It is independent of nerve supply.

Examining the evidence, it becomes apparent that the wheal is the only part of the tissue response which owes its existence to only one major factor, namely, blood flow.

The histamine wheal test, clinically practical because of producing grossly visible wheals, is based on this reasoning. The appearance of wheals indi-

cates reasonable blood flow, and the time of appearance and size of the wheal gives a relative estimate as to the amount of that flow. In this hospital we have used the histamine wheal test for several years, and have preferred it to others as a practical and roughly reliable test for the extent and degree of vascular impairment. However, it is time-consuming, painful, potentially dangerous and open to errors in reading and interpretation. Moreover, it represents a forced response of tissue to strong stimulation.

If a method were known whereby the wheal reaction to a less forceful, smaller, and painless source of irritation, such as a scratch, could be definitely and simply demonstrated, the accuracy and reliability of the wheal test would be enhanced and the objections to it largely abolished. The intravenous fluorescein ultraviolet fluorescence method of Lange has been discovered to be the answer to this problem. Quite by accident, during the routine fluorescence examination of a severely impaired leg, it was noted that minute areas of trauma made immediately before injection of the fluorescein appeared brilliantly fluorescent from thigh to upper calf, and were completely nonfluorescent below. The general skin fluorescence was present to the tips of the toes and absent only where actual gangrene was present.

Careful investigation of the *modus operandi* of this phenomenon has shown that scratch fluorescence appears only when a wheal response occurs. The following facts have shown this to be true:

1. Intravenous fluorescein is injected and allowed to circulate for two to three minutes. A tourniquet is then applied to the arm and the intravascular pressure is allowed to equalize. A scratch is then made below the tourniquet. The "red" reaction appears as usual in the scratch, but inspection under special light reveals no fluorescence. The tourniquet is then released and the fluorescence soon appears in the scratch marks. Therefore, the red reaction itself is not responsible for fluorescence. Furthermore, if it were responsible, all scratches should fluoresce regardless of vascularity since this element is independent of blood flow.

2. Scratch fluorescence is not due to the "flares" since this element is irregular and spread out from the area of injury, whereas the fluorescence is limited to the scratch. Furthermore, obvious flares made by intradermal injection of histamine do not appear fluorescent.

3. When a histamine wheal is made, followed by intravenous injection of fluorescein, the area of the wheal is seen to be brilliantly fluorescent.*

The test therefore, offers a simple way of determining the ability of tissue to produce minute, grossly invisible wheals to mild, painless surface scratches. Since wheal formation is entirely dependent on active vascular flow, the effect of the test is to measure the point distal to which vascular flow falls below a critical level. Absence of fluorescence reveals an incomplete repair response and consequently must indicate delayed ability to heal. This fact is further

* This discovery was made by Nathanson¹¹ and used by him for measuring circulation time in any part of the body. We have used this procedure as an improved method of reading the regular histamine wheal test for peripheral vascular disease. However, we discarded this in favor of the scratch method for reasons mentioned above.

substantiated by observation of the scratch marks under ordinary light, five to seven days after the test. At this time, it can be readily seen that the marks above the level of absent fluorescence are practically healed, whereas below this level they are still in the process of healing (Fig 1). Other clinical data points to the veracity of this interpretation.

EQUIPMENT

Fluorescein — Fluorescein (resorcinophthalein) is a readily available, inexpensive non-toxic acid dye, first employed intravenously by Erlich¹³ in 1822 and applied clinically since then in many fields^{14, 15, 16, 17, 18}. Though several forms of fluorescein have been used for this purpose, our experience is limited to the use of a 20 per cent solution of sodium fluorescein in distilled water, autoclaved in 50 to 100 cc colored dispensing bottles for 15 minutes and given in 5 cc doses. This solution is stable and easily made. When injected intravenously, it diffuses rapidly into the tissue fluids. Its intensity depends not only on dosage, but apparently also on the protein content

of the body fluids—since it is brilliant in inflammatory exudates and poorly visualized in edema of stasic origin¹⁹. The dye is rapidly excreted by the kidneys and secretory glands in unchanged form. Clinically, it produces an icteric tint to the skin for two to three days, colors the urine and body secretions for three to four days, and causes false positive urine sugar tests for four to five days. Fluorescein should probably not be given to cases with severe kidney damage associated with significant nitrogen retention. Fluids should be forced for two to three days after injection in all cases. No serious com-

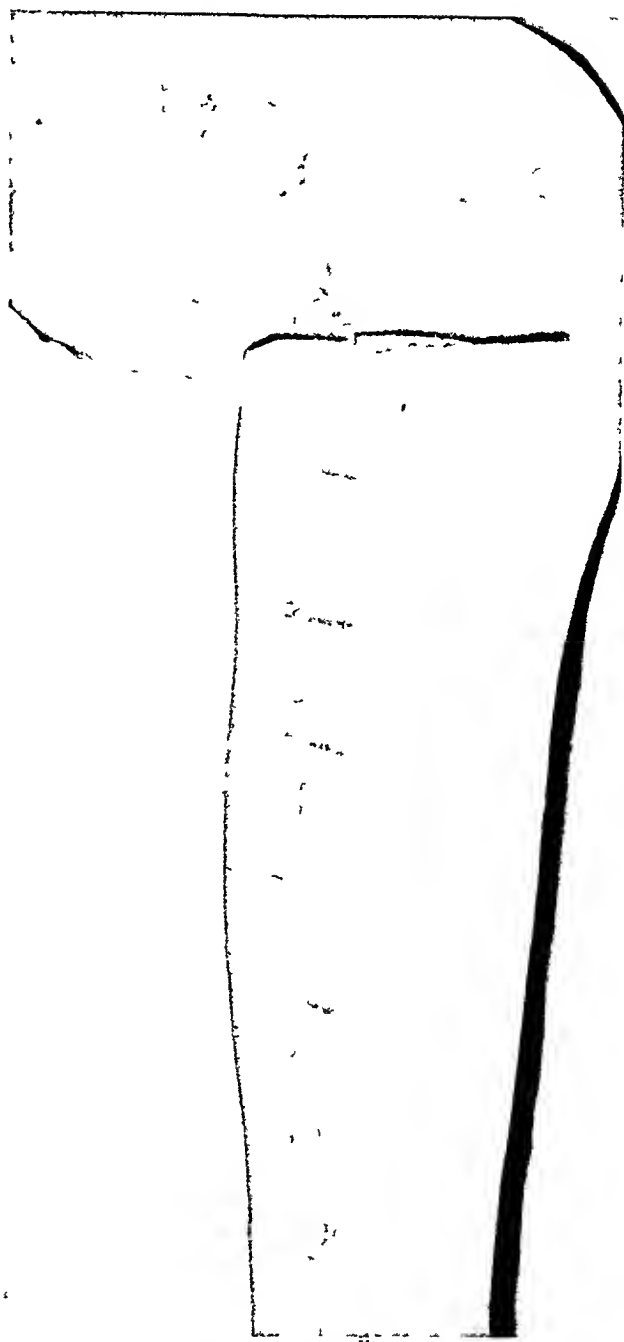


FIG 1—(Photograph taken five days after testing.) Note the delay in healing of the scratches below the inked mark where scratch fluorescence disappeared. The last two marks above the line showed decreased fluorescence.

¹⁹Wheal fluid has approximately the same protein content as blood serum (Lewis)

plications have ever been reported from the intravenous use of fluorescein in spite of extensive experience in many clinics. The only complication we have seen is the occasional occurrence of slight nausea during injection.

Filtered Ultraviolet Light—It has long been known that special short wave light reveals characteristic fluorescence in certain substances. Lange showed that light with a wave length of from 3600 to 3800 Angstrom units reveals the optimum luminescence of fluorescein. A source of ultraviolet may be made to transmit waves of this frequency by the addition of a purple filter (Corning glass No 587-Lange) or the special filter designed for this purpose by Wood,¹⁹ and known by his name. We have used a Mazda AH4 mercury vapor bulb set in a projector housing with a condensing focus lens,[†] as our source of light. The small purple glass filter is clipped inside the housing at the point of light passage into the condensing lens. The housing is mounted on a triangle stand with screw clamps to allow movability. A General Electric autotransformer is incorporated on the base of the stand to step up the voltage sufficiently to allow the bulb to function. The light so obtained is very effective in revealing surface fluorescence. Though various other, and some less expensive units have been suggested by others, we have had no experience with them, and feel that it is important to have a standard and adequate source of this special light for good results. Many additional clinical uses for this type of light have been described, and it is particularly valuable in the fields of ophthalmology²⁰ and dermatology.²¹

TECHNIC

The patient is wheeled into a room which can be darkened. The legs are exposed from low thigh to the toes. The inner or outer aspect of the entire leg and foot on both sides is prepared by washing with alcohol. A series of superficial scratches are made at two-inch intervals down the legs in comparable places. The lowest scratch mark can be made at the base of the toes on the dorsum of the foot. It is rarely important to go farther than this, since such detail of information is not necessary. The scratches are made by repeatedly (five to ten times) stroking the skin in the same spot with an hypodermic needle. They do not have to be deep, and do not have to draw blood. A little experience with the method quickly reveals how to make these marks evenly. They can be placed to avoid obvious areas of dermatitis and inflammation. As soon as the marks are completed, five cubic centimeters of 20 per cent sodium fluorescein solution is injected intravenously at a normal rate. The room is darkened, and, without delay, the filtered ultraviolet light is played upon the scratched area. The test can be read within one to two minutes, which is just about the time necessary to darken the room and allow ultraviolet light to reach its peak intensity. The test does not change appreciably after this period and remains readable for over an hour.

† Made by the Central Scientific Company of Chicago

METHOD OF READING TEST

The major fact to observe is the level at which the marks cease to be fluorescent. If present, this change is always abrupt and easily seen. Some patients show another type of level, marked by a definite decrease in intensity of scratch fluorescence. This should also be noted and may occur alone or in combination with a lower level where fluorescence disappears. General luminescence of the skin of varying intensity can be seen in the background but never interferes with reading the scratch test, since the latter areas are much more intense and localized.

DISCUSSION—While experience with the method is not large enough for conclusive statements, correlation to clinical examination, other known tests, and end-results point to the fact that scratch fluorescence gives reliable factual data regarding the degree and extent of vascular impairment. Further correlations are underway and a later paper is planned to more carefully evaluate this data.

Before presenting the conclusions which can be drawn from the test, it must be carefully emphasized that the information obtained by this technic concerns only the vascular situation. While the importance of this data is not to be underiated, it should never be used as a sole criterion for treatment, for it answers only one of the many questions of equal importance to be considered in this decision. Some of these other factors are: The age of the patient, his general health, his mental condition, his neuromuscular ability, his desire for or against amputation, his economic situation, his occupation, the presence or absence and degree of gangrene, the presence or absence of infection and/or osteomyelitis, the degree of sepsis, and the type of vascular disease presented. There is no test good enough to obviate the necessity for careful clinical judgment and individualization of cases. With this well in mind, the following conclusions can be drawn regarding the significance of the test. They should be used as clinical aids, and not solutions of the problems presented.

1 When scratch fluorescence is present to a certain level, and absent distal to that point, severe organic vascular impairment exists below the last fluorescent mark sufficient to seriously affect the ability of the tissue to repair itself. Though local and general treatment without leg amputation may be attended by healing, the result is likely to be only temporary, and requires prolonged hospitalization. (See Case 1)

2 When scratch fluorescence is equally and brilliantly present in all marks, significant organic vascular disease does not exist in the tested areas. Vasospastic disease apparently does not affect the test, and may be predominantly responsible for symptoms in these cases. (See Case 2) If gangrene is present distal to the last fluorescent mark at the base of the toes, the process is shown to be largely a local one. Local and general treatment with removal of necrotic areas are apt to be followed by healing and return to good function. (See Case 3)

3 When scratch fluorescence is present throughout, but of definitely

decreased intensity below a certain point, a graded degree of vascular disease exists. Immediate prognosis under local and general treatment is good, but ultimate prognosis is guarded (See Case 4).

4 Amputation in areas of absent scratch fluorescence is likely to be followed by poor or absent healing requiring re-amputation at a higher level (See Case 5). Amputation in areas of decreased fluorescence is hazardous (See Case 6).

CASE SUMMARIES

Case 1—H E, a 66-year-old male, entered the Wisconsin General Hospital with infected gangrene of the left great toe, lymphangitis, and abscess formation in the lateral midcalf area. Pulsations on the affected side were absent in the popliteal, posterior tibial, and dorsalis pedis arteries. On the right, pulsations were absent in the posterior tibial and dorsalis pedis arteries. Scratch fluorescence was absent below the tibial tubercle of the affected leg, and present in all marks on the good leg, though of decreased intensity below the tarsometatarsal joint area. The impression was that of severe organic arterial insufficiency below the tibial tubercle on the left and significant but not critical impairment in the right foot. In view of a careful study of all other factors bearing upon the case amputation was advised at the low thigh level. This was refused by the patient. Conservative treatment, including drainage of the abscess, was instituted. The infection began to clear and improvement was noted. The scratch fluorescence test was repeated one week later and showed no change. Amputation was again advised and refused. Continuation of therapy and surgical removal of the gangrenous toe were carried out. Four weeks later, the leg appeared to have greatly improved. The infection had cleared, and the pain was gone. However, the surgical wound remained unhealed. The scratch fluorescence test was again repeated and showed improvement in circulation since scratch fluorescence was now present to the supramalleolar level. However, it was of definitely decreased intensity between the tibial tubercle and the malleoli, and absent below this point. Conservative treatment is being carried on and we believe that eventual healing will occur under optimum conditions. However due to the extent and degree of the disease, we expect this healing to be temporary and feel that the patient will return shortly after resuming normal activity because of persistent and progressive difficulties. The case illustrates the delayed healing which was indicated by the scratch fluorescence test and also demonstrates the value of the test as a method of detecting improvement under treatment.

Case 2—E Z, a 65-year-old diabetic woman, entered the Wisconsin General Hospital because of pain, coldness, numbness, and impaired function of the left leg. Examination revealed both legs to be cool and slightly moist. No gangrene was present, and pulsations were palpable in all arteries. Scratch fluorescence was promptly, equally, and brilliantly present in both legs from the thigh to the ends of the metatarsals. Predominant vasospastic disease was diagnosed, and treatment with heat, massage, and mecholyl resulted in relief of symptoms and return to function. From this case and others like it, it appears that scratch fluorescence is not affected by vasospastic disease.

Case 3—H D, a 57-year-old diabetic male, entered the Wisconsin General Hospital because the local area where several gangrenous toes had previously been removed by chemosurgery²² had failed to heal. The pulsations in the arteries of this leg were absent in the popliteal, posterior tibial, and dorsalis pedis arteries. In the opposite leg the posterior tibial and dorsalis pedis pulsations were absent. There was an indolent ulcer at the site of previous chemosurgical treatment. Roentgenograms revealed osteomyelitis in the ends of the two metatarsal bones underlying the ulcer. The question was raised as to the proper course of therapy, and amputation of the leg was recom-

n ended A scratch fluorescence test was done and fluorescence was present to within one inch of the ulcer It was present and of good intensity throughout the opposite leg but was decreased in intensity in the lower one-half of the foot Local removal at a slightly higher level was consequently suggested and performed including the infected bone Healing has progressed rapidly and the patient is nearing the time for his discharge In this case, leg amputation was prevented because the reason for poor healing was shown to be predominantly local

Case 4—A B, a 65-year-old white male, entered the Wisconsin General Hospital because of increasing coldness and paresthesia in the right foot and intermittent claudication of the right leg Examination revealed definite decrease in temperature on the right as compared to the left leg, extending to mid calf All pulsations were present except the right posterior tibial and dorsalis pedis Scratch fluorescence was present in all marks of both legs and feet, but from mid calf down on the right, they were definitely less brilliant than the opposite leg Significant, though not critical vascular tissue starvation of the right leg was diagnosed Conservative treatment resulted in moderate improvement, and he was discharged If he follows instructions, a considerably long period of activity will be afforded him However, we expect his arterial disease to gradually become more severe and necessitate his return for more drastic treatment The ability of the test to show lesser degrees of vascular impairment is demonstrated

Case 5—J W, a 63-year-old female, had been a patient in this hospital one year prior to the present entry At that time, diagnoses of malignant hypertension, general arteriosclerosis, and bleeding gastric ulcer were made A gastric resection was done During her convalescence, she began to develop gangrenous ulcers of her left foot and calf Pulsations were absent below the left femoral The disease progressed, and amputation was done by the Callander technic The wound failed to heal at that level, and reamputation at midthigh was necessitated She was discharged following uneventful healing and returned one year later because of pain, coldness, numbness, and paresthesia of the remaining leg No gangrene was present Pulsations below the femoral were absent There was speculation as to whether a Callander amputation could be done on this side (conservative treatment having failed) Scratch fluorescence was present to the level of the adductor tubercle on the right thigh and absent below this, showing that Callander amputation would have met the same fate as it had previously when done on the left leg Midthigh amputation was done Though we have no case in which amputation was deliberately done in an area of absent scratch fluorescence, this case illustrates by inference the probable results

Case 6—W McL, a 66-year-old man, had previously been a patient in the Wisconsin General Hospital because of Buerger's disease Chemosurgical removal of a gangrenous ulcer had been performed, but not attended by complete healing He returned for further treatment Scratch fluorescence was present to the immediate supramalleolar level, but absent below There was also a level at the tibial tubercle, below which the scratch fluorescence was decreased in intensity It was decided to try a calf amputation This was followed by healing of the suture line, but a pressure necrosis ulceration over the area of the beveled edge of the tibial stump occurred The low resistance of the tissue there allowed this to reach considerable size before debridement and local measures checked it Healing was progressing well though at a somewhat reduced rate when it was decided that the best result would follow reamputation at the supracondylar level This was done with prompt healing This case illustrates the poor results of local treatment in areas of absent fluorescence and also the somewhat impaired healing ability in areas of decreased fluorescence

It must be emphasized that, though the test indicates the lowest level of amputation likely to be attended by prompt healing, it is not to be concluded

that such a level or its vicinity is necessarily the site of choice. We feel strongly that aged, decrepit patients should have an amputation (when necessary) at a level not only where healing will occur, but where it will be permanent. To amputate these cases below the knee is to court trouble, and offers no particular advantage. On the other hand, in younger persons with greater reserve who require amputation, the test affords a method of selecting the lowest feasible level, and allows better functional results. Though certain of these cases may require later reamputation, they have been afforded a more active life in the interim, and are better able to stand a second operation.

SUMMARY

A new, simple, and apparently reliable test for extent and degree of vascular insufficiency is introduced. Its component parts are described, and their bases in logic discussed. The equipment necessary, and the technic of performance are presented. Clinical considerations are outlined with cases to support them. It is recommended that other clinics adopt the procedure and further analyse its possibilities. A later paper is planned in which a more exhaustive evaluation will be presented.

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POOLED HUMAN SERUM*

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DURING THE PAST FOUR YEARS, the medical literature has contained many articles dealing with the advantages of pooled human plasma as a blood substitute. In England and Canada, the use of pooled human serum has been extensive, experiences with serum in the United States, however, have been limited to a small number of observers, and, this, despite the favorable results published in the English journals. The present paper is a report on the administration of 297 units of human serum to 136 different patients.

Experimental Background—The therapeutic efficacy of serum in shock has been firmly established. Best and Solandt³ produced shock in 70 dogs by three different methods: (1) histamine administration, (2) skeletal trauma, and (3) extensive hemorrhage. Their dogs were under nembutal anesthesia. Hematocrits, blood volume determinations (blue dye method), and serum proteins were done. Some animals were in shock from three to five hours. They found that, whereas, injections of adrenalin and pituitrin were ineffective, and dextrose and saline were temporarily effective, infusions of serum were followed by recovery in 60 out of 70 dogs. Bond and Wright⁶ induced shock in 31 dogs by manipulation of the intestine, by trauma, and by bleeding. The blood pressure was kept between 50 and 60 mm of mercury for one-half to two hours before therapy was started. Controlled and saline infused dogs all died rapidly, whereas, dogs treated with serum lived for the duration of the experiment. Magladery²² states that serum and plasma are equally effective in treating experimentally induced shock, but that *concentrated* serum is no better than isotonic serum. George Whipple,³¹ in plasmaphoresis experiments, showed that when the red cells were suspended in dog's serum and re injected "the toxic effect of the plasma depletion is removed. Thus blood serum proteins are stabilizing or protective factors. This may be their most important function."

That serum is effective, likewise, in correcting shock in humans is attested to by numerous observers. Bick,⁵ in Australia, Best and Solandt,⁴ in Canada, Hayes,¹⁵ in India, and many workers in England are enthusiastic about the use of serum.^{8, 9, 10, 28} In the United States, however, the pendulum has swung so far over in favor of plasma that clinical experience with serum is more limited. Elliott,¹² Hughes, Mudd, and Strecker,^{16, 17} Levinson,^{20, 21}

* This article is based wholly upon observations made at the Presbyterian Hospital, New York, N Y, before Captain Edward B Self entered active military service.

Much of this paper is a condensation of a thesis submitted by Captain Edward B Self in partial fulfillment of the requirements for the degree of Doctor of Medical Sciences, Columbia University, New York, N Y, awarded in May, 1943.

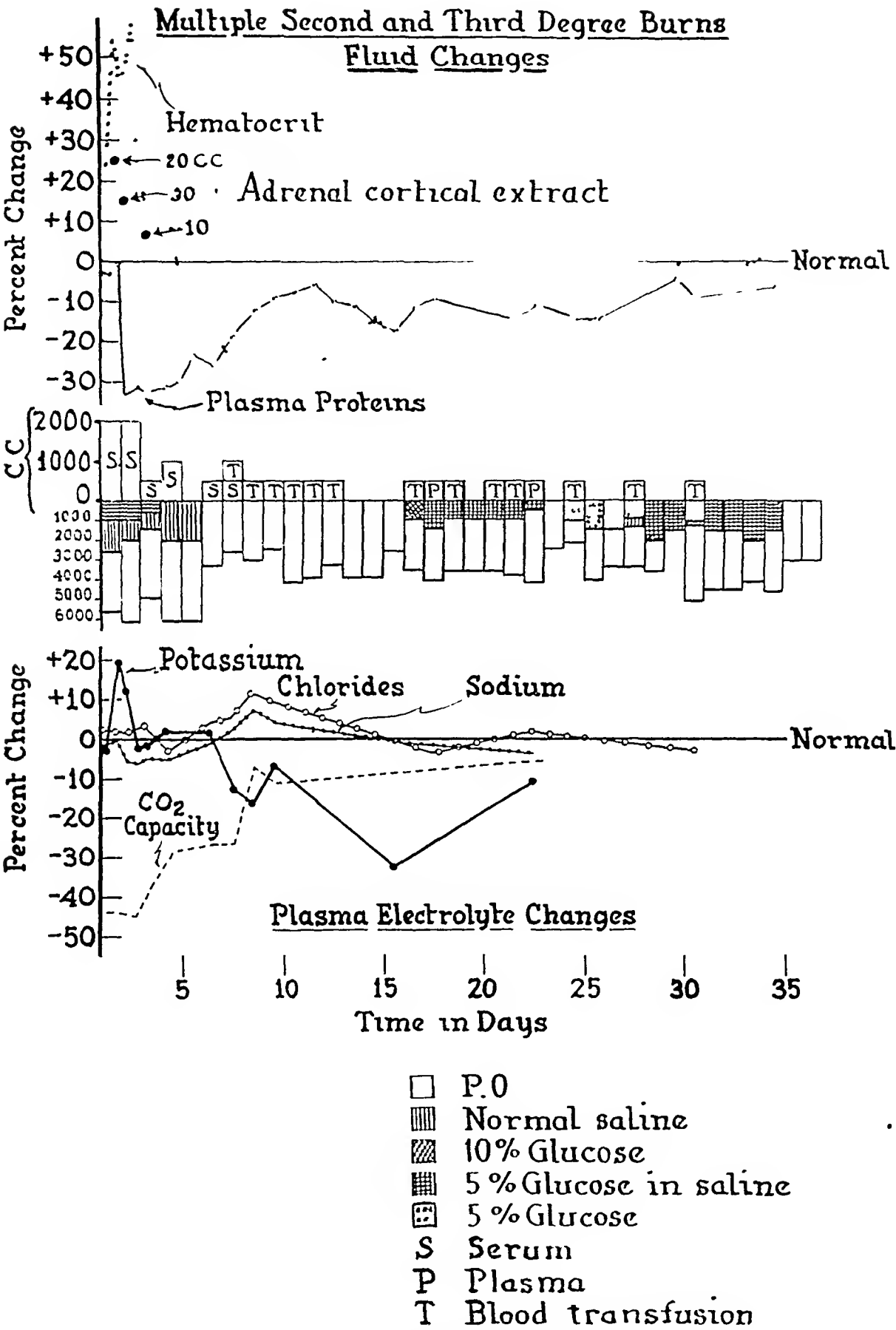


FIG 1 —(Reproduced from Scudder, J, and Elliott, R. H. E, Jr, South Med and Surg, 104, 651 658, 1942)

Necheles,²³ and Strumia²⁹ have used serum fairly extensively, and some experience has been had by others^{11, 14} Hyland¹⁸ prefers serum in transfusing children because the sodium citrate in plasma may combine with calcium to cause tetany. The consensus of opinion appears to be that serum is equally as effective as plasma, although associated with a higher incidence of reactions.

Our series includes 49 cases of shock. The response of these patients to serum infusion was excellent and, as might be expected, was exactly the effect one would have anticipated from an equal amount of plasma.

The liquid serum was provided by Dr. William Thalhimer, of the Manhattan Convalescent Serum Laboratory. Blood was obtained for this project from American Red Cross donors. Prerequisites for blood donations were a negative history for syphilis, malaria and recent infectious disease, normal temperature, hemoglobin over 80 per cent, normal pulse and blood pressure.

Five hundred cubic centimeters of blood were drawn into a sterile bottle and clotting allowed to occur. Under sterile technic, the clot was cut into four parts and allowed to stand overnight in the refrigerator so that maximum retraction could take place. In the morning, after centrifuging, all serum and loose cells were drawn off and again centrifuged. Only clear supernatant serum was now withdrawn. This was tested for contamination and the serum held for seven days in the refrigerator until the bacteriologic tests assured sterility. Only serologically-negative serum was used. Enough serum was now pooled to make up nine liters (from approximately 45 donors) and further sterility tests were done. Merthiolate was added to make a dilution in the serum of 1-10,000. The pools were then filtered through 10- x 3-inch Mandler filters, and the serum was drawn for final sterility tests after which the ampoules were sealed with a blow torch. The proportion of the blood groups in the largest pool was: blood group O —48, group A —38, group B —8, and group AB —4.

Dried serum was supplied through the cooperation of Dr. C. P. Rhoads, of the Memorial Hospital, New York. It was prepared from the frozen state by the method of Folsom,¹³ at Doctor Thalhimer's laboratory.

Analyses of the electrolyte content of serum pools were done for sodium, potassium, carbon dioxide, and chloride. All figures were within normal range (except for CO₂, which was low). The protein content of the serum pools as determined by the micro-kjeldahl method was between 6.8 and 7.0 grams per cent. This contrasted with a figure of 4.5 to 5.5 grams per cent for many plasma pools tested. The higher protein concentration of the serum is, of course, due to the fact that no anticoagulant and diluent had been employed.

All infusions were given without previous cross-matching, and with no consideration paid to the blood group of the particular patient. In the early months, when concern was held for possible severe reactions, the pulse, respiration, blood pressure, and rectal temperature of the patient were recorded before, during, and after administration, and in some cases,

electrocardiograms were done After the giving of serum, rectal temperatures were taken every hour for four to six hours Late reactions were watched for Venous pressure readings were measured before, during, and after some infusions Blood samples were drawn immediately before, 10 to 60 minutes after, and 24 hours after giving of serum Hematocrit and plasma proteins²⁴ were done on these samples, and in many instances the concentration of sodium, potassium, chloride, and carbon dioxide capacity were determined²⁷ With few exceptions the serum was given *via* infusion sets which had been cleaned by a strict technic and which were autoclaved within four hours to eliminate, as far as possible, pyrogenic contamination Later in the study, blood bank infusion sets were used, and no increase in the rate of reactions was noted

The total number of units of serum transfused was 297, all but a few of the units being in 500 cc amounts The quantity of serum administered at a single injection varied from 50 cc in a few babies to a maximum of 4000 cc in a burn case The total amount given in several infusions to one patient was 5850 cc The average dose of serum per case was 580 cc

UNITS OF SERUM USED

Liquid, pooled	196
Fresh (1-2 days)	5
Dried pooled	85
Fresh (5 days)	2
Concentrated (3 times)	6
Miscellaneous	3
	<hr/>
Total	297

THE CLASSIFICATION WITH THE DISTRIBUTION OF CASES

1 Shock cases	48
a. Due to skeletal trauma	3
b. Due to hemorrhage	19
c. Due to dehydration	7
d. Operative and postoperative shock	18
e. Due to blood transfusion	1
2 Burn cases	15
3 Septic cases	14
4 Hypoproteinemia	22
5 Prophylactic (before and after operation)	22
6 Miscellaneous	15
	<hr/>
Total cases	136

Shock Due to Skeletal Trauma—The three patients in this group had multiple compound fractures One was bleeding from the external auditory meatus, and had obvious cerebral injury He died shortly after arrival, while serum was still being transfused The second case lived after amputation through the condyles of humerus for compound fracture The third case (age 70) died 24 hours later Autopsy revealed a fractured skull with laceration of the brain

Shock Due to Hemorrhage—Nineteen cases were included in this category In general, these patients were benefited by serum therapy Six died,

four from continued bleeding within 12 to 36 hours after serum (laceration of aorta, bleeding esophageal varices, wound of the vena cava *etc*) All except two had either transfusions of whole blood or red blood cells

The lowest hematocrit in this series to survive was 16.5 per cent The smallest amount of serum required for treatment was 250 cc, the largest 1500 cc, with the average being 750 cc

The following case is illustrative

DIAGNOSIS RUPTURED ECTOPIC PREGNANCY

NO 633812 Y G

Date	2/15/41	2/15/41
Time	12 30 PM	2 20 PM
Hematocrit	23.8 %	21.3 %
Plasma proteins	6.0 Gm %	6.5 Gm %
Plasma sodium	134.4 mEq /L	132.1 mEq /L
Plasma potassium	3.7 mEq /L	3.7 mEq /L
Plasma chlorides	105.3 mEq /L	105.0 mEq /L

Therapy 400 cc normal saline and

500 cc serum given before operation

400 cc serum during operation

500 cc blood after reaching ward

Remarks Patient in shock Given saline followed by serum before and during operation Shock responded well Convalescence uneventful

Shock Due to Dehydration—Seven cases fall in this class In these states serum and salt are the medications of choice Transfusions of whole blood may be contraindicated because of the elevated cell volume The following is presented as an example of several we have seen, *ie*, dehydration shock suddenly occurring in a patient where the loss of fluid and base from an enterostomy, or fistula, is not properly evaluated Such collapse is often unsuspected because the urinary excretion appears to be adequate, and it is erroneously assumed that the state of hydration is satisfactory

DIAGNOSIS COMMON BILE DUCT FISTULA

NO 627438 N B

Date	4/22/41	4/22/41	4/26/41
Time	9 00 AM	3 30 PM	10 00 AM
Hematocrit	50.3 %	33.5 %	25.5 %
Plasma proteins	10.2 Gm %	8.1 Gm %	6.7 Gm %
Plasma sodium		127.4 mEq /L	132.6 mEq /L
Plasma potassium	7.2 mEq /L	6.9 mEq /L	4.9 mEq /L
Plasma chlorides		104.1 mEq /L	111.3 mEq /L

2000 cc
5% dextrose
400 cc serum
clysis of
3000 cc
5% dextrose
in saline

The magnitude of hemoconcentration is not appreciated from the hematocrit alone and illustrates the necessity of simultaneous plasma protein determinations This case also shows the characteristic increase in potassium concentration together with the typical decrease in sodium concentration associated with base depletion—in this instance due to loss of bile

Clinically For two days before collapse, the patient was mentally confused and drowsy, with dull eyes and cold extremities Following treatment with fluids and serum, her skin became warm and her general condition immediately improved

Operative and Postoperative Shock—Of 18 patients in this group all

but one are recorded as showing improvement following serum. The indication for therapy was a falling blood pressure during a prolonged operative procedure or during the postoperative course. The systolic blood pressure was usually below 80 when therapy was begun. Blood studies after serum demonstrated the expected hemodilution together with a fall in plasma protein concentration.

TABLE I

*Hemo- *Hema- *Plasma *Plasma *Plasma *Plasma *Plasma *Whole Blood *Cell
globin tocrit Proteins Sodium Chlorides CO₂ Potassium Potassium Potassium
(Gm %) (%) (Gm %) (milliequivalents per liter) (milliequivalents per liter)
Combining Power

Normal values		14 5	47 0	7 0	142 0	103 0	27 0	4 40	50 0	103 0
Days	Time									
1	6 40 AM	18 6	57 4	6 77	139 7	104 8	14 7	4 28	55 6	93 8
	10 20 AM	21 8	70 7	6 77	141 0	107 0		4 50	67 9	94 2
	1 05 PM	20 1	66 2	6 97	142 4	105 4		14 5	5 25	64 7
2	7 45 AM	23 2	73 0	4 59	134 7	103 9		4 92	67 5	90 6
	1 30 PM	18 3	57 3	4 80	132 3	104 7	14 4	4 24	57 7	97 5
3	8 30 AM	16 8	51 5	4 69	134 2	106 1	16 4	4 29	50 2	93 5
4	8 00 AM		52 2	4 76	133 7	98 7	18 9	4 53		
6	7 30 AM		38 2	5 14	139 3	107 4	19 2	4 45		
7	9 30 AM	11 2	33 8	5 61	146 0	108 1	18 8	3 81	35 0	96 1
8	10 45 AM		33 0	6 16	153 0	115 0	24 4	3 67	36 8	104 2
9	3 00 PM		32 7	6 33	148 2	112 3	23 2	4 07	37 0	104 8
15	1 00 PM		36 4	5 75	141 9			2 92		
22	4 00 PM	12 2	38 9	6 19	136 0	103 9	25 0	3 92	45 9	111 8

*Venous blood

(Reproduced from Scudder, J., and Elliott, R. H. E., Jr., *South Med and Surg.*, 104: 651-658, 1942)

Burns—Our experience with serum in burns is limited to 15 cases, but this small number is outweighed by the excellent clinical response and by the fact that serum was used in the treatment of a patient with the highest hematocrit to survive (73 per cent). The amounts of serum given varied from 500 cc to 5850 cc (the latter being equivalent to that obtained from 24 donations of blood). In many instances, serum was supplemented with plasma and later with blood. There were three deaths. One, a six-year-old colored child received only 500 cc of serum, and died 24 hours following the accident. The second death resulted from a lung abscess eight weeks after admission. The third death occurred five hours after injury. When examined this patient was in an alcoholic stupor and had received burns involving 60 per cent of his body surface.

The following schema illustrates the relevant facts concerning blood chemistry and therapy of D. R. No. 644068. His hemoconcentration (hematocrit 73 per cent) was extreme and he responded in a gratifying way to massive injections of serum.²⁵

Notes on Case

1. Despite 4000 cc of serum and 12,000 cc of other fluids he still had an hematocrit of above 70 per cent at the end of 60 hours.

2. Elevated potassium and lowered sodium and carbon dioxide capacity occurred in the early period after the burn.

3 The rise of plasma proteins following massive injections of serum and blood was slow

4 Initial hemoconcentration was followed by anemia requiring 13 transfusions of whole blood

5 In 30 days he received the equivalent in blood, serum and plasma of 43 donors. Such therapy was out of the question a few years ago before the establishment of blood banks

Septic Cases—The 14 cases were predominantly ones of generalized fibrinopurulent peritonitis. These patients showed a progressive trend toward hemoconcentration and hypoproteinemia. Serum proved temporarily helpful, but, unless the underlying pathology (bowel perforation, drainage of abscess, etc.) was corrected, the prognosis was always poor.

Use of Serum Prophylactically and for Hypoproteinemia—Forty-four patients were given serum as a prophylactic measure. This is the second largest group, and illustrates that, in a general hospital, serum will be employed chiefly in correcting disturbed nutritional states associated with hypoproteinemia, shock, and burns. Example

DIAGNOSIS STENOSING DUODENAL ULCER AGE 77

NO 510917 W P

Date	Time	Amount of Serum	Hematocrit	Plasma Proteins
2/26/41	11 AM		30.8%	4.8 Gm %
2/26/41	10 mins after serum	1000 cc	32.4%	6.0 Gm %
2/28/41	10 AM		31.6%	5.8 Gm %
2/28/41	2 PM	1000 cc	29.2%	6.5 Gm %

NOTE Adequate amounts of serum have to be given to raise the plasma protein level. As a rule, too small doses are injected. This case received 140 grams of serum proteins to increase the concentration from 4.8 grams per cent to 6.5 grams per cent.

IS SERUM SAFE?

The relative toxicity of serum is a disputed point. Reports in the literature vary from those who consider serum to be extremely toxic, even fatal, to those who claim to have used large amounts with no evidence of reaction. Table II will illustrate the variation in opinions.

TABLE II

Date	Author and Reference	Remarks
1896	Weiss ³⁰	Serum for all species of animals is invariably toxic, often fatal.
1900	Brodie ⁷	Intravenous injection of serum into cats causes respiratory arrest and stoppage of the heart. These effects are absent if vagi are cut. The active substance in the serum is a proteid, of the albumen class and is only produced when blood clots. Serum obtained from plasma is inactive.
1918	Janeway ¹⁹]	Injected blood serum causes serious vasoconstriction. The responsible substance is not a protein but is a crystalloid. Although present in coagulated blood it is not dependent upon the actual formation of the blood clot with the possible exception of thromboplastin.
1940	Clegg ¹⁰	Has given many serum infusions and as much as 1600 cc at one time. Only one reaction (chill) noted.
1940	Aldrich ²	Reactions from four-times concentrated serum—"insignificant."
1940	Levinson ²¹	No reactions noted in 47 patients.
1941	Bick ⁵	Three mild reactions in 16 cases.
1942	Elliott ¹²	One reaction in 23 cases.
1942	Sharpey-Schafer ²⁸	Has given large amounts of serum (2100 cc in 17 minutes) to many cases. Only reaction is "occasional mild wheals."
1943	Ackroyd ¹	Has given 2012 units of serum to over 800 patients. No evidence of serum toxicity. Reaction rate four per cent.

POOLED HUMAN SERUM

REACTION RATE IN THIS SERIES

In the present series of serum transfusions, the reactions are graded as follows

- Grade 0 (None)
- Grade 1 (Hives, itching, *etc*)
- Grade 2 (Rise of 1° F, rise of 2° F in febrile cases)
- Grade 3 (Chill and fever)
- Grade 4 (Collapse, cyanosis, severe lumbar or chest pain, *etc*, requiring stopping of infusion or supportive treatment)

TABLE III
POOLED HUMAN SERUM
REACTIONS

Type of Serum	Number of Transfusions	Grade 1	Grade 2	Grade 3	Grade 4	Total	Per Cent
Liquid, aged 2 months	157	3	9	18	7	37	
Fresh (1 day old)	4			4		4	
Fresh (2 days old)	1			1		1	
Total	162	3	9	23	7	42	25.9
Dried aged	71		10	8	1	19	
Fresh (5 days old)	2			1		1	
Total	73		10	9	1	20	27.4
Concentrated, 3 times (liquid)	6	1			2	3	50.0
Miscellaneous (refiltered)	3			2		2	66.7
Total	244	4 (1.6%)	19 (7.8%)	34 (13.9%)	10 (4.1%)	67	27.5
Total excluding fresh concentrated, and miscellaneous	228	3	19	26	8	56	24.6
Type of plasma							
Liquid plasma	157	2	2	1	2	7	4.5
Dried plasma	71	0	2	2	1	5	7.0
Total	228	2	4	3	3	12	5.3

Although in most instances it was a simple matter to determine the presence or absence of a reaction, this was not always so. Certain patients received transfusions of whole blood immediately before or after serum. A reaction in such a case would be difficult to evaluate. Such cases are not counted in Table III.

In febrile patients, it was often a matter of opinion as to whether or not the infusion of serum was followed by a real febrile response. The statistics in Table III are, therefore, accurate only within the limitations and observations of the person judging the reaction.

The incidence of reaction was 27.5 per cent for the 244 transfusions of serum. There was little difference between the reaction rate for the liquid and dried product. From this study there are certain deductions:

1. Fresh liquid serum gave consistently 100 per cent chill-fever reaction rate. This lends credence to the earlier observations of Brodie,⁷ and Jane-

way¹⁹ What this toxic factor is in fresh serum which disappears on aging is not known. It is however of no clinical significance because today, fresh serum can not be given due to the time limitation imposed for determining the sterility of both the pool and the final container.

2 Liquid serum prepared by concentrating in cellophane bags gave such severe reactions in three of the six patients that the remaining seven bottles were not used. Electrophoretic patterns done on this material revealed changes in both the albumin and globulin fractions.²⁵

3 The chill-fever reaction (Grade 3) constituted the largest group, 13.9 per cent. If the reactions due to fresh serum, concentrated liquid serum, and reworked serum are deleted, this reaction rate drops to 10.7 per cent.

4 The ten severe reactions (Grade 4) which required stopping of the serum transfusion or immediate supportive therapy included two which occurred while giving the concentrated liquid serum described above. One was characterized by a drop in blood pressure to 60/40, dyspnea, pain in the neck, back, loins, and about the heart and was relieved by adrenalin. The second, a nephrosis case, had such severe pain in the chest, kidneys, and back after 30 cc that the infusion was discontinued and adrenalin injected. Five serum transfusions were stopped because of a shaking chill developing during its administration and two others because of lumbar pain.

A phlebotomy with removal of 300 cc of blood was necessary immediately after an infusion of 1000 cc of serum. This case, one of an aortic aneurysm, received serum 11 days after wiring of the aneurysm. Just at the end of the infusion the patient became orthopneic, cyanotic, and developed wheezing respiration together with signs of cardiac failure. The phlebotomy relieved the condition.

It is not wholly correct to blame serum alone for some reactions because certain individuals are known to be reactors. Example: One patient was given serum six days after closure of a disrupted wound. The serum was stopped within two minutes because of severe lumbar and nuchoid pain. Skin tests later showed hypersensitivity to the serum and the reaction was classed as anaphylactic. The remainder of the above serum (400 cc) was injected the next day into a burn case without any untoward effects. Two other patients who developed chills with serum also had chills following whole blood transfusions.

There was no fatality in this series attributed to the giving of serum. Reactions practically never occurred in patients being treated for shock. This is of practical significance.

The total reaction rate, excluding the fresh, the concentrated liquid, and the reworked serum, was 24.6 per cent.

In conclusion, it should be stated that giving of this serum is associated with a significant incidence of reaction, but that this incidence is not high enough nor are the reactions severe enough to warrant withholding the use of serum as a blood substitute.

BLOOD SUBSTITUTES

SUMMARY SHEET

Albumin
Liquid Plasma
Dried Plasma

Others
Liquid Serum
Dried Serum

Name _____ Age 45 Group AB Unit No 684005
Sex M Color W Ward KE
G. P. Hospital Presbyterian

(surname) (given) 420

Diagnosis Acute enteritis due to Salmonella Serial No S-206-207

Type of Case Surgical, Medical, Fracture, Urological, Obstetrical, Gynecological
(underline) Ward, Semi-private, Private

Reasons for plasma, serum, etc Total Amount 1,000 cc

Shock due to dehydration from diarrhea. Admitted in profound shock with blood pressure 20/0, cold and cyanotic. Peripheral veins collapsed. Clysis given because of inability to do venepuncture.

Final disposition of patient improved, unimproved, dead, autopsy
(underline) Admitted 8/1/42. Transferred to Medicine 8/2. Discharged 9/3/42

Date	8/1/42	8/2/42	8/3/42	8/4/42				
Time	7:45 PM	9 AM	9:15 AM	11:35 AM				
Before, During, After Infusion, Transfusion, Clysis (state)	After clysis 1500 cc.	serum 1000 cc.						
Whole Blood Sp Gr								
Hematocrit	57.7%	43.6%	42.4%	45.0%				
Plasma Sp Gr	1.0358	1.0263	1.0255	1.0280				
Plasma Proteins	9.83	6.60	6.33	7.18				
Na								
K								
Cl								
CO ₂ Capacity								
Others	Hgb. 17.5	12.5	14.5	14.6				
	RBC 6130000	3580000	5040000	4240000				
	WBC 7920	4440	8700	6240				

Remarks regarding effect of material on blood chemistry Prompt blood dilution with fall in the hematocrit and plasma proteins

Clinical results of each Vein cut down on and needle tied in. 1,000 cc. of serum run in rapidly. transfusion

1,500 units of adrenal cortical extract injected i.v. This was followed by 2000 cc of saline. B.P. rose to 130/100 within four hours after admission. Response excellent. Shock did not recur.

ANALYSIS OF PLASMA OR SERUM GIVEN

Lot number	S18-E89						
	S17-E76						
Source	Dr Thalhimer						
Type (specific)							
Group							
Pooled	yes						
Date drawn							
Date pooled							
Date given	8/1/42						
Age in days							
Amount given	1,000 cc						
Concentration							
Isotonic	yes						
Hypertonic							
Dilute							
Amount of Diluent							
Given Time	4 30 PM						
Alone	yes						
Before, During, or After (state)	After						
Saline	1,500 cc						
Glucose							
Transfusion							
Eschatin	Before 60 cc						
Others							
Operation							
Delivery							
REACTION							
Grade 0	yes						
(None)							
Grade 1							
(Hives, itching, etc.)							
Grade 2							
(Rise 1° F, 2° in sepsis)							
Grade 3							
(Chill and fever)							
Grade 4							
(Collapse, cyanosis, etc, requiring stopping of infusion or supportive Rx)							

REMARKS

Excellent response The serum was followed by 2,000 cc. of saline infusion.

SERUM *versus* PLASMA

The writers wish to emphasize at this point that we hold no brief for either one of these blood substitutes as opposed to the other. We believe that each has a place in the treatment of patients and that the blood bank of the future will dispense both substances. Personal experience with the use of dried and liquid pooled plasma on similar types of patients has been had, and it is fair to say that plasma and serum are equally efficacious clinically. They can be used interchangeably without noticeable difference. The chemical similarity and like origin of each makes it at once illogical to assume striking differences between them. It is true, however, that each possesses certain advantages which the other does not.

A comparison of 157 transfusions of liquid serum with 157 of liquid plasma and 71 transfusions of dried serum with an equal number of dried plasma reveals a significant difference in reaction rate—24.6 per cent for serum and 5.3 per cent for plasma (Table III).

ADVANTAGES

Plasma

- 1 Lower incidence of reactions
- 2 Greater yield (2–4 per cent ?)
- 3 Contains fibrinogen and prothrombin
- 4 More easily prepared as a by-product of a blood bank. Blood can be used as blood or later processed into plasma

Serum

- 1 Greater protein content, pools contain 7 grams per cent compared to 5 grams per cent for plasma
- 2 Obviates expense and trouble of citrate
- 3 Can be filtered, hence bacterial sterility can be assured
- 4 Liquid serum remains clear, plasma (unless recalcified) precipitates out fibrin
- 5 Drying is easier without presence of citrate

SUMMARY AND CONCLUSIONS

Pooled human serum is an effective blood substitute. Its therapeutic value has been demonstrated in the treatment of patients with various types of shock, burns, and hypoproteinemia, and as supportive measure in the sick and debilitated.

Approximately 297 units of serum were given intravenously to 136 patients.

Serum administration is associated with a definite incidence of reaction, greater than with plasma. In this series the reaction rate was 27.5 per cent. Fresh serum, prepared and injected within 24 hours of the drawing of the blood, gave a severe chill and fever response in each case.

Serum and plasma are equally efficacious and the reactions each causes are rarely severe, the choice between them becomes largely a question of convenience and practicability of preparation and administration.

Serum is now being prepared at the Presbyterian Hospital Blood Bank to meet the need of supportive therapy in patients with low plasma proteins and low calcium. Massive replacement with serum rather than with citrated plasma theoretically is safer in such states, particularly in infants.

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PLASMA VOLUME, "AVAILABLE (THIOCYANATE) VOLUME" AND TOTAL CIRCULATING PLASMA PROTEINS IN NORMAL ADULTS*

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MUCH ATTENTION has been devoted to the elucidation and establishment of the importance of (1) extracellular dehydration, (2) reduced plasma and blood volume, and (3) hypoproteinemia and protein depletion in such conditions as hemorrhage, traumatic shock, burns, intestinal obstruction and fistula, acute and chronic starvation, *etc*. There have been numerous attempts to use laboratory methods for the quantitative measurement of the body deficits in order to aid in their more accurate correction in the patient. Empirical rules have been formulated for blood transfusion based upon the hematocrit or the erythrocyte count, NaCl and water administration based upon the plasma chloride concentration, plasma replacement based upon the hematocrit, plasma protein concentration, *etc*. Inasmuch as all these rules may work fairly well in special instances and to the detriment of the patient in other instances, we can expect more attempts to formulate better criteria. As a matter of fact, this study is the outgrowth of an attempt to formulate a grid to make possible more accurate quantitative replacement of body fluids and simple enough for general clinical use, with an accuracy not being limited to any special type of clinical condition. Furthermore, it was hoped especially that the *degree of protein depletion* of a patient could be measured by the simultaneous determination of plasma volume and plasma albumin concentration and by comparison with normal standards to estimate quantitatively the extent of protein depletion.

In studies dealing with nutritional hypoproteinemia in the dog, Weech and his coworkers,^{1, 2} and Sachar, Horvitz and Elman³ noted that the loss of total circulating plasma albumin was a small but relatively constant part of the total nitrogen lost, and our own observations have led to somewhat the same conclusion.⁴ It occurred to us that in patients with hypoproteinemia, associated primarily with malnutrition, a knowledge of the deficit of total circulating plasma albumin might be of aid in evaluating approximately the extent of body protein depletion. In other words, in patients following periods of protein starvation the simultaneous determination of the plasma volume and the plasma albumin concentration should give values from which, by comparison with normal standards, the extent of dehydration and protein depletion could be evaluated more accurately.

It is evident that the success of the foregoing approach to the problem depends not only upon a reasonably constant relationship between the decline

* Aided by a grant from the John and Mary Markle Foundation

of the total circulating plasma albumin and the loss of tissue protein during a period of inadequate protein intake but also upon reasonably constant levels of the plasma volume and total circulating plasma albumin in normal persons with the same physical measurements. The primary object of the present study was, therefore, to determine the constancy of the plasma volume and of the total circulating plasma albumin in normal adults of the same

RELATIONSHIP BETWEEN PLASMA VOLUME AND SURFACE AREA

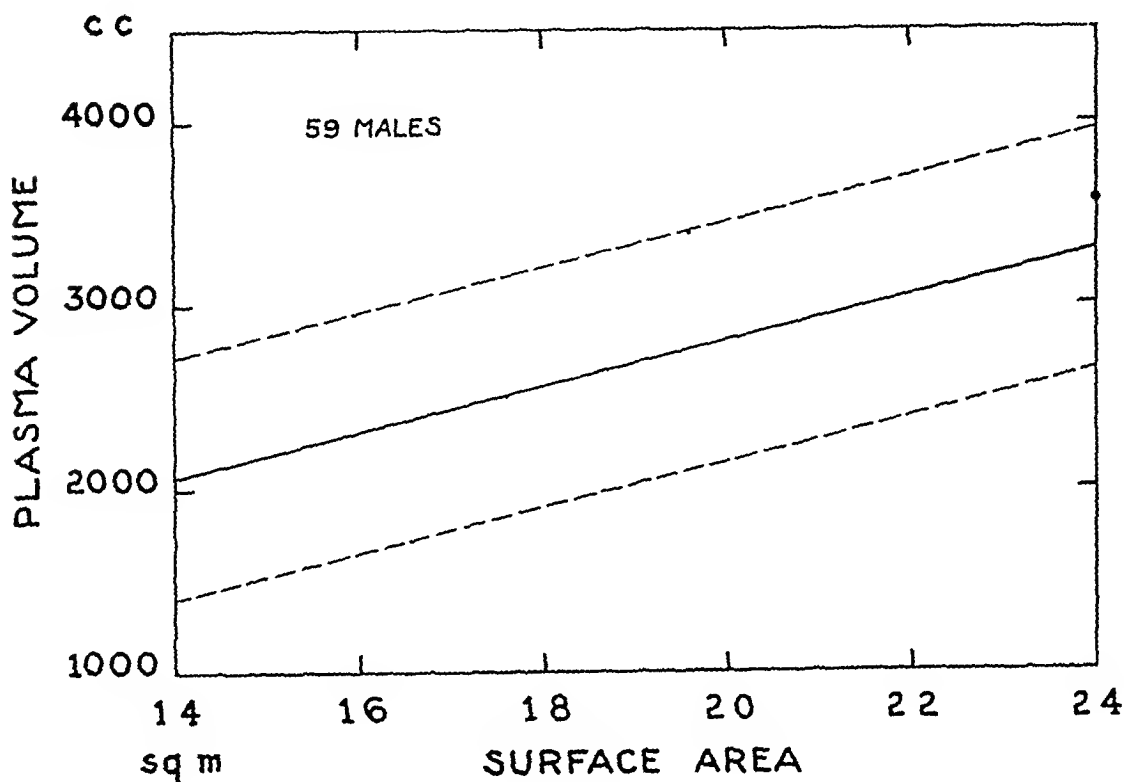


CHART 1

physical measurements. To this end, plasma volume and plasma protein determinations were carried out on a series of 63 normal male and 14 normal female subjects. Simultaneous determinations of the "available (thiocyanate) volume," hematocrit and plasma chloride were also performed.

METHODS

The determinations of the plasma volume and of the "available (thiocyanate) volume" were made by the direct method of Giegerson and Stewart⁷ as adapted to the photo-electric colorimeter by Gibson and Evelyn.⁸ The subjects, for the most part medical and dental students, were studied routinely in the morning approximately three hours after a light breakfast and immediately after a one-hour lecture. The breakfast was essentially fat-free, consisting of a glass of fruit juice, two pieces of dry toast with jelly and one cup of black coffee or its equivalent as water. The subjects were recumbent during the entire experimental period. The antecubital vein of one arm served for the withdrawal of the control blood sample and the

injection of the test substances. The antecubital vein of the other arm was used for the withdrawal of three experimental blood specimens, at 15-minute intervals after the time of injection. The blood was withdrawn with minimal stasis, employing lubricated syringes. The drawn blood was immediately discharged into 15 cc centrifuge tubes containing heparin as the anti-coagulant. The tubes were stoppered tightly and centrifuged at 2500 r p m for 20 minutes. The plasma specimens were then transferred to other stoppered tubes and centrifuged again for 20 minutes at the same rate.

TABLE I
COMPOSITION OF THE BLOOD OF NORMAL MEN AND WOMEN

		Number of Observations	Mean	Standard Deviation	Minimum	Maximum
Men						
Total plasma protein	Gm per 100 cc	63	6.62	0.35	5.8	7.3
Plasma albumin	Gm per 100 cc	62	4.72	0.33	4.2	5.3
Hematocrit	per cent	63	48.2	2.5	42	53
Plasma chloride	m Eq /L	59	101.5	2.1	96	107
Women						
Total plasma protein	Gm per 100 cc	14	6.53	0.31	6.0	7.2
Plasma albumin	Gm per 100 cc	12	4.62	0.33	4.0	5.2
Hematocrit	per cent	14	42.3	2.3	38	47
Plasma chloride	m Eq /L	14	101.4	2.3	99	106

The concentration of the dye in the plasma at "zero" time was obtained by linear extrapolation of the density values for the three 15-minute experimental plasma samples against time. The mean of the density values obtained with the second and third experimental plasma samples (30 and 45 minutes after injection) was employed to calculate the plasma concentration of thiocyanate.

A portion of the control blood specimen was used to determine the hematocrit value, in duplicate and undiluted, with the aid of Van Allen hematocrit tubes. Pooled plasma from the four blood specimens was used for the protein and chloride determinations. Total plasma protein and plasma albumin were determined by micro-Kjeldahl, employing the technic of Robinson, Price and Hogden⁷ for globulin filtration after precipitation with 22.2 per cent sodium sulfate solution. Chlorides were determined by the method of Wilson and Ball.⁸

RESULTS

The results of the blood determinations carried out on the present series of normal adults, 63 males and 14 females, have been summarized in Table I. It will be noted that the values fell within the same ranges of variation for normal adults as have been reported by a number of laboratories. The findings for males and females exhibited no significant differences except in the case of the hematocrit readings which were definitely lower in the females.

Scatter diagrams, as illustrated in Charts 1, 2, 3 and 4, were prepared from the data collected on the male subjects to show the relationship between plasma volume, "available (thiocyanate) volume," total circulating plasma protein and total circulating plasma albumin on the one hand and the body surface on the other. It will be observed immediately that in each instance

there was a considerable scattering of the points. The solid line in the center of each diagram represents the calculated line of regression, indicating the trend of the several values to increase with an increase in the body surface*. In order to show the range of variation to include the respective values of 95 per cent of all normal adult male subjects, the broken lines in each figure were constructed on the basis of the line of regression taking plus or minus two standard errors of estimate from the line of regression. Since the

RELATIONSHIP BETWEEN AVAILABLE (THIOCYANATE) VOLUME AND SURFACE AREA

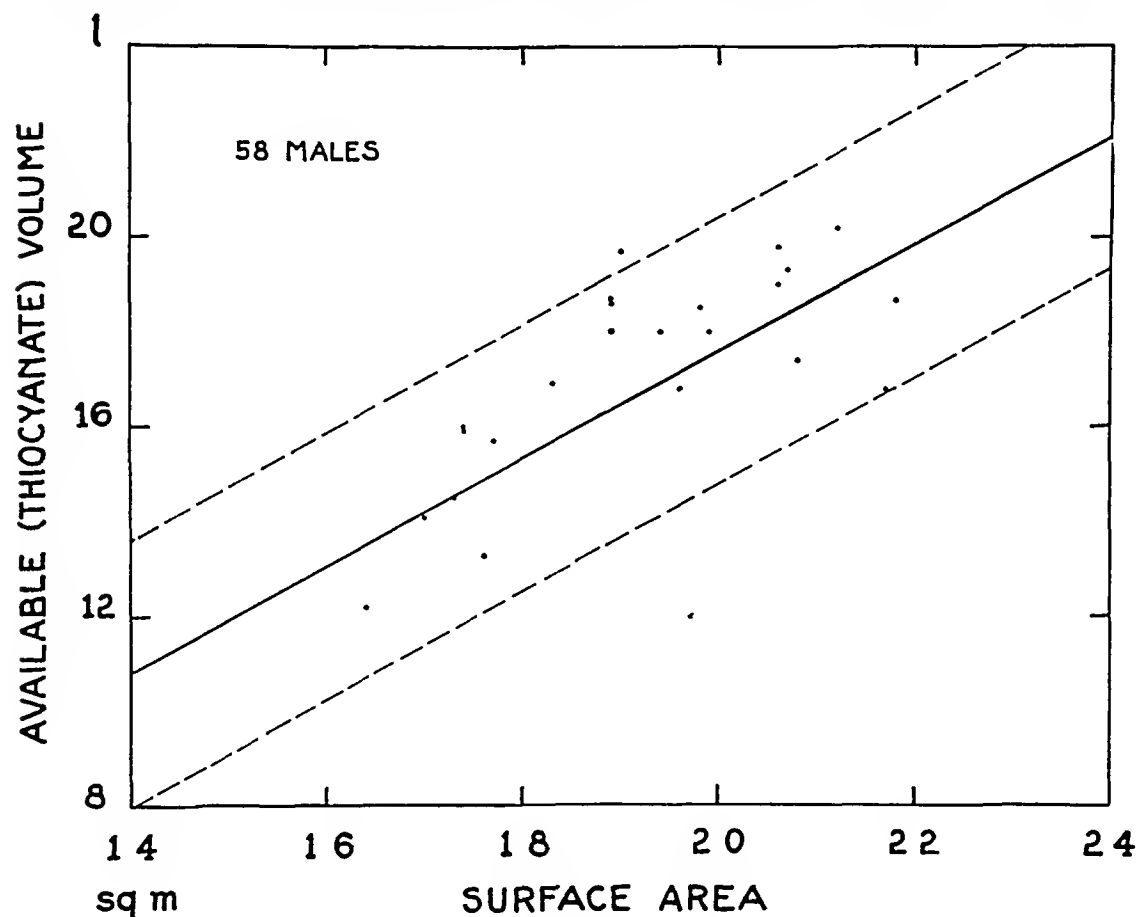


CHART 2

number of subjects is small and the range of body surface is comparatively narrow, this method of analysis of the data is not entirely free from criticism statistically. On the other hand, it should serve to indicate the ranges of variation which one can expect with the methods employed for the various determinations in given adults of the same physical measurements. Thus, in the case of the relationship between the plasma volume and body surface, the line of regression plus or minus two standard errors of estimate, or the line of regression ± 655 cc, includes 95 per cent of the values for all normal adult males. Stated in another way it will be seen from Chart 1 that for a man

* The method of least squares as outlined by Snedecor⁹ was used in calculating the line of regression.

with a body surface of 1.90 square meters, the normal plasma volume range with 95 per cent certainty, would be approximately from 2000 to 3300 cc

TABLE II

RELATIONSHIPS BETWEEN BODY FLUIDS AND VARIOUS PHYSICAL MEASUREMENTS IN NORMAL MEN

	Area Sq. M	Weight Kg	Height Cm
Plasma Volume			
Number of observations*	59	59	59
Mean physical measurement	1.90	73.16	176.8
Mean plasma volume cc	2686	2686	2686
Plasma volume cc/unit of body size	1414	36.72	15.19
Regression coefficient† cc	1244	22.27	23.12
Standard error of estimate‡ cc	327.6	336.0	340.8
Standard error of estimate x 100 — mean plasma volume	12.20	12.51	12.69
Available (Thiocyanate) Volume			
Number of observations*	58	58	58
Mean physical measurement	1.88	71.97	175.8
Mean available (thiocyanate) volume in liters	16.24	16.24	16.24
Available (thiocyanate) volume liters/unit of body size	8.64	0.226	0.093
Regression coefficient † liters	11.30	0.185	0.185
Standard error of estimate‡ liters	1.41	1.59	1.65
Standard error of estimate x 100 — mean available (thiocyanate) volume	8.68	9.79	10.1

* Three of the plasma volume values (two of available (thiocyanate) volume) are averages of two determinations of the subjects
† The increase in plasma volume (or available (thiocyanate) volume) per unit of physical measurement
‡ Standard deviation from the line of regression

TABLE III

RELATIONSHIP BETWEEN CIRCULATING PLASMA PROTEINS AND VARIOUS PHYSICAL MEASUREMENTS IN NORMAL MAN

	Area Sq. M	Weight Kg	Height Cm
Total Circulating Plasma Protein			
Number of observations*	59	59	59
Mean physical measurement	1.90	73.16	176.8
Mean circulating protein Gm	177.8	177.8	177.8
Circulating proteins Gm/unit of body size	93.58	2.43	1.00
Regression coefficient† Gm	71.20	1.078	1.246
Standard error of estimate‡ Gm	23.68	24.46	24.14
Standard error of estimate x 100 — mean circulating protein	13.32	13.76	13.58
Total Circulating Plasma Albumin			
Number of observations*	57	57	57
Mean physical measurement	1.90	73.11	176.6
Mean circulating albumin Gm	125.8	125.8	125.8
Circulating albumin Gm/unit of body size	66.21	1.72	0.71
Regression coefficient† Gm	60.22	0.997	0.945
Standard error of estimate‡ Gm	17.32	18.11	19.11
Standard error of estimate x 100 — mean circulating albumin	13.77	14.40	15.19

* Three of the observations are averages of two determinations on the subjects
† The increase in total circulating plasma proteins (or albumin) per unit of physical measurement
‡ Standard deviation from the line of regression

When a similar consideration was given to the relationship between the "available (thiocyanate) volume," total circulating plasma protein and total circulating plasma albumin on the one hand and body surface on the other, the ranges of deviation from regression with 95 per cent certainty were found to be ± 2.8 liters ± 47.4 Gm and ± 34.6 Gm, respectively. Thus, the approximate normal ranges would be "Available (thiocyanate) volume" 1300 to 1900 liters, total circulating plasma proteins 130 to 225 Gm, total circulating albumin 90 to 160 Gm

The statistical analysis of the data for the male subjects on the relationships between the body fluids and circulating plasma proteins and the various physical measurements has been summarized in Tables II and III. By focusing attention on the per cent that the standard error of estimate* represents of the several mean values, it will be seen that the best correlation with physical measurements was encountered with the "available (thiocyanate)

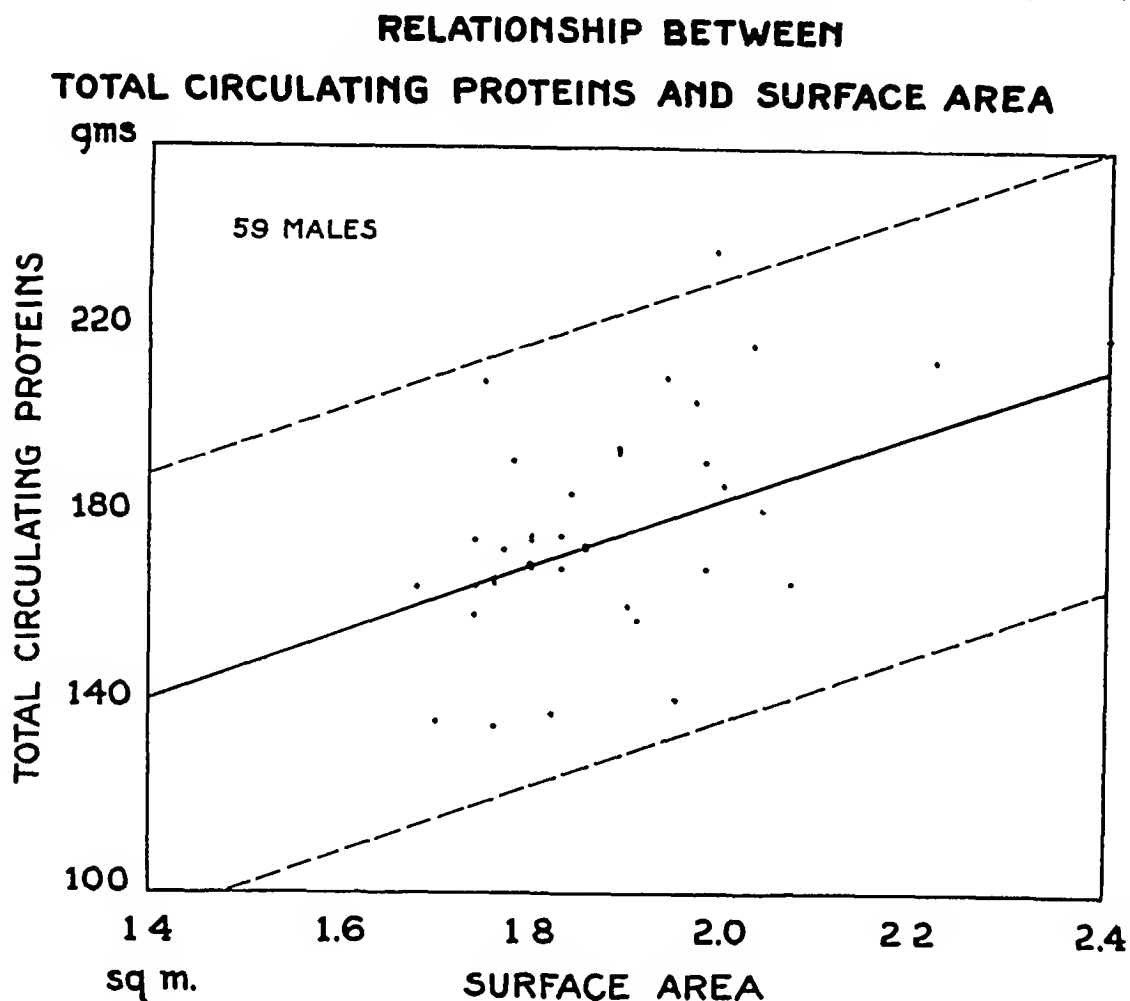


CHART 3

volume," followed in order by the plasma volume, total circulating plasma protein and total circulating plasma albumin. Further, a similar comparison of the magnitude of the standard error of estimate with respect to the mean values for the various physical measurements reveals little if any significant difference in the case of plasma volume and in the case of the total circulating plasma protein. On the other hand, in the case of the "available (thiocyanate) volume" and the total circulating plasma albumin, the closest correlation was encountered with body surface, followed in order by weight and height.

Since only 14 female subjects were studied, a similar analysis of the data was not attempted. Suffice it to state that all the values for the plasma volume, "available (thiocyanate) volume" and total circulating plasma

* The standard error of estimate is the standard deviation from the line of regression and includes 67 per cent of all normal values.

proteins obtained with the female subjects fell within the ranges of variation encountered for the males

The blood volume was calculated employing the plasma volume and the hematocrit. A scatter diagram showing the relationship of the blood volume to surface area showed that the deviation was approximately as great as that noted in the relationship of plasma volume to surface area.

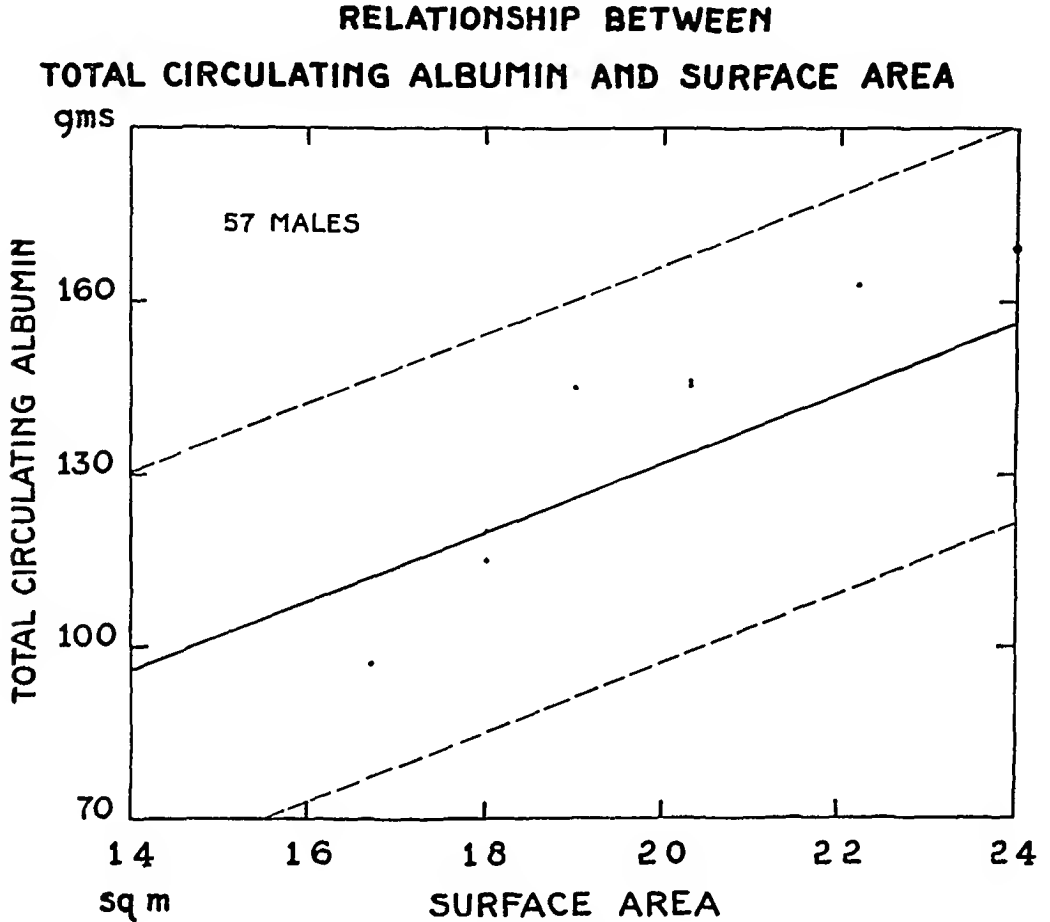


CHART 4

COMMENT

From the present study it would appear that in normal adult males a slightly better correlation may be found with body surface than with either height or weight when consideration is given to the relationship between plasma volume, "available (thiocyanate) volume," total circulating plasma protein or total circulating plasma albumin on the one hand and physical measurements on the other. It would also appear, however, that a considerable range of variation in the values may be encountered in normal adults of the same physical measurements. Thus, from the data presented in Table II, the expected range of plasma volume variation with 67 per cent certainty for a man of 1.90 square meters body surface and a mean plasma volume of 2686 cc was found to be ± 327.6 cc, while the

expected range of "available (thiocyanate) volume" variation with 67 per cent certainty for a man of 188 square meters and a mean "available (thiocyanate) volume" of 1624 liters was found to be ± 141 liters. Similarly, from Table III, the expected range of total circulating plasma protein variation with 67 per cent certainty for a man of 190 square meters body surface and a mean total amount of circulating plasma protein of 1778 Gm was found to be ± 2368 Gm, while the expected range of total circulating plasma albumin variation with 67 per cent certainty for the same person having a mean total amount of circulating plasma albumin of 1258 Gm was found to be ± 1732 Gm. In this connection, it might be pointed out that in their series of normal subjects Gibson and Evans¹⁰ noted that the differences in plasma volume of individuals of comparable age, sex, height and weight may be considerable.

Although the number of subjects studied in the present report was admittedly small and the physical measurements fell within a comparatively narrow range, the variations encountered in the plasma volume and the total amount of circulating plasma albumin in subjects of the same physical measurements preclude their usefulness as intended, that is, the possible deviations were found to be so great that in a patient with malnutrition a clinical evaluation of the extent of dehydration and of protein depletion with any degree of certainty would be questionable, if based upon a comparison of the determined levels of the plasma volume and the total amount of plasma albumin with the respective so-called normal standards. The data obtained lead to the conclusion that the chief clinical value of the plasma volume and the total circulating plasma albumin determinations lies in observing the changes of these factors in a given subject during a test period.

SUMMARY AND CONCLUSIONS

Determinations of the plasma volume, "available (thiocyanate) volume" total circulating plasma protein and total circulating plasma albumin were carried out in 63 normal adult males and 14 adult females. The various values were related to body surface, weight and height. The study was carried out with the object of establishing normal levels for the plasma volume and the total amount of plasma albumin, on the assumption that a knowledge of the deficits of plasma volume and total circulating plasma albumin might aid in evaluating, clinically, the extent of dehydration and the degree of protein depletion in patients with hypoproteinemia associated primarily with an inadequate protein intake. The results and conclusions may be briefly presented as follows:

1. For normal adult males, the relationships between plasma volume, "available (thiocyanate) volume," total circulating plasma protein or total circulating plasma albumin on the one hand and physical measurements on the other revealed a slightly better correlation with body surface than with either weight or height.

2 Rather wide ranges of variation of the foregoing factors were encountered in normal male subjects of the same physical measurements. From statistical analysis of the data, the expected ranges of plasma volume and the total circulating plasma albumin variation, with 67 per cent certainty, for a man of 1.90 square meters body surface having a mean plasma volume of 2686 cc and a mean total amount of circulating plasma albumin of 125.8 Gm were found to be ± 327.6 cc and ± 17.32 Gm, respectively.

3 These ranges of variation are of such a magnitude that a clinical evaluation, with any degree of certainty, of the extent of dehydration and of protein depletion in patients following periods of protein starvation would be questionable, if based upon a comparison of single observation of levels of the plasma volume and the total amount of circulating plasma albumin with the respective normal levels.

4 The determinations of plasma volume and total circulating plasma albumin would appear to find their principal usefulness in observing changes in these factors during a given test period by serial determination.

5 All the values for the plasma volume, "available (thiocyanate) volume" and total circulating plasma proteins determined on the 14 female subjects fell within the ranges of variation encountered for the males.

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MALIGNANT GRANULAR CELL MYOBLASTOMA INVOLVING THE URINARY BLADDER

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THIS IS A REPORT of a granular cell myoblastoma involving the urinary bladder which exhibited the histologic characteristics of a benign neoplasm in its primary manifestation and yet metastasized widely, causing death.

It seems necessary to identify the tumor which we choose to call granular cell myoblastoma and explain the reason for using this name, which is not the one most commonly employed. The tumor type was first described by Abrikossoff, in 1926, and called by him myoblastic myoma (myoblasten-myom). In 1931, he published a second paper in which he described the histologic features of four different varieties of the tumor: (1) The typical form made up of round, egg-shaped, or elongated myoblasts from 20 to 25 microns long with granules but without longitudinal or cross striations, (2) a variation of the first type in which some cells show longitudinal or cross striations, (3) an hypertrophic form with cells from 40 to 160 microns and sometimes multinucleate. These first three groups are all composed of granular cells and all are benign tumors. (4) Malignant myoblastic myoma in which the myoblasts are not granular, but assume atypical aspects and vary in size so that the tumor resembles a polymorphous sarcoma. He had no personal experience with this fourth group but cited the case of von Meyenburg as an example of it.

The observations of Abrikossoff have been repeatedly confirmed but most unfortunately subsequent authors have elected to use the term myoblastoma indiscriminately for all four of Abrikossoff's groups without emphasizing the important histologic and clinical distinctions between the first three benign groups and the fourth malignant group.

This omission becomes serious when Howe and Warren warn us that myoblastoma is more often malignant than is generally supposed, since five of their ten cases behaved like malignant tumors, without making it perfectly clear that all of the malignant tumors belonged to Abrikossoff's fourth group of myoblastomas.

Indeed, until the case here reported was observed by us we were firmly convinced that no example of a malignant primary granular cell myoblastoma belonging to any of Abrikossoff's first three groups had ever been recorded. None of Howe and Warren's malignant cases do so, nor do any of the ten malignant cases which they have culled from the literature. One of us (A P S) has studied these ten cases and is convinced that none of them, in its primary manifestation, belonged to Abrikossoff's first three groups. In Morpurgo's second case, the *metastases* resembled the metastases of the case we are about to report but the primary tumor was quite different.

We feel, therefore, that tumors belonging to Abrikossoff's first three groups, since they are almost all benign, should be labelled clearly with a distinctive name so that they will not be confused with the other forms of striated muscle tumors most of which are malignant. For this reason we choose to use the name "granular cell myoblastoma." This is not new, since it has already been employed by Lattes and Horn and Stout, and it appeals to us as eminently reasonable and necessary. It is beyond the scope of this paper to discuss the propriety of using the term myoblastoma for Abrikossoff's fourth group, but we may be permitted to regret that he ever chose to include it with his first three groups since it has provided such a potent source of confusion.

Case Report—D Y, white, male, age 31, single, a pressman, was first seen by one of us (A R) on March 29, 1943. According to the mother he had been a deaf mute since the age of one when he had cerebrospinal meningitis. In 1937, he had had osteomyelitis of the left ankle following injury, for which he was operated upon twice. He had had diurnal frequency every two to three hours and nocturia at least once for many years. There had been painless hematuria, with urinary frequency every hour, for 11 days before admission.

Physical Examination—The subject was a young deaf mute, quite emaciated and anemic. The heart was normal in size, with a pounding apex beat and loud sharp systolic and rough diastolic murmurs heard over the aortic and pulmonic valves. The lungs were clear. The abdomen was scaphoid in type. Liver, spleen and kidneys were not felt. A large, very firm, smooth, nontender mass was felt in the lower abdomen as far up as the level of the anterior iliac spine, extending on the right to the iliac and pubic bones and into the true pelvis. B P 120/54. The urine was port wine in color and essentially negative except for the blood. Rectal examination revealed a very large, firm, immobile, smooth mass filling almost the entire true pelvis and more prominent on the right than on the left. The upper limit of the tumor mass could not be reached by palpation through the rectum. Preliminary roentgenograms of the kidneys and bladder showed obliteration of the kidney outlines by gas. There was a rather wide separation of the symphysis pubis. Attempt at cystoscopy failed. A No 21 F sound could be passed but was deflected far to the left. Rectal palpation, with the sound in the urethra, showed a normal prostate and left seminal vesicle. The large mass palpated to the right of the prostate was highly suggestive of an unusual type of tumor that appeared to arise from either the right lateral lobe of the prostate or the right seminal vesicle. A No 16 F Coude rubber catheter was passed into the bladder and only a small amount of slightly blood-tinged urine was withdrawn. The patient was immediately sent to the Adolph Hospital, with a tentative diagnosis of an unusual giant-sized sarcoma involving the bladder, prostate and right seminal vesicle.

At the hospital an intravenous pyelogram, reported by Dr Asa B Friedman, revealed a functionless right kidney. The left renal function was normal and the pelvis showed slight hydronephrosis. The lower third of the left ureter was lifted upward by a deformity of the bladder (Fig 1). The crescentic-shaped bladder was markedly deformed by a large, smooth, regular, oval mass that filled the major part of the bladder area and seemed extrinsic to the bladder. The bladder itself showed a small capacity and was pushed far upwards and to the left, overlying the left anterior superior spine of the ilium. A roentgenogram of the chest was negative.

The blood showed 62 per cent Hb, R B C 3,210,000, W B C 9,400, 76 per cent polys, 19 per cent lymph, 5 per cent mononuclear. Blood sugar 95.4 mg per 100 cc, urea nitrogen 158, creatinin 1.3.

Owing to the unusual type and size of the tumor mass a celiotomy was considered



FIG 1.—Intravenous pyelograms to show progress of the tumor. The one at the left was taken March 30, 1943—before operation. The right kidney is functionless, the left normal except for slight hydronephrosis. The bladder outline is semilunar and pushed far to the left. The center pyelogram was taken May 17, 1943—six weeks after operation. The bladder now appears more normal in contour and location. The pyelogram at the right was made May 5, 1944—13 months after operation. The bladder is pushed upwards and its pear shape indicates encroachment around its neck and base. The lower end of the left ureter has a bizarre relation to the bladder neck. The kidney findings remain essentially unchanged.

preferable to a perineal approach, even though it was thought at the time that we were dealing with a sarcomatous tumor arising from the right seminal vesicle

Operation—April 1, 1943 (A R and R A R) Under spinal anesthesia, a midline incision extending from the umbilicus down to the symphysis pubis was made. The tumor mass was exposed and found to be smooth, well encapsulated, of hard rubbery consistency, heart-shaped, and about the size of a large grapefruit. It was tightly wedged into and filled the entire right iliac fossa, the right false and true bony pelvis and pressed against the sacrum. At its contact with the urinary bladder, which was thinly stretched across the upper left border of the tumor, the neoplasm lost its distinct demarcation which characterized the rest of the mass and apparently merged imperceptibly with the musculature of the bladder which was torn into during the enucleation of the tumor from this area. The entire mass was carefully enucleated from its surrounding tissue bed by blunt dissection. A number of large vessels leading directly into the mass were ligated and cut. A tiny area which was intimately adherent to the upper part of the right external iliac vein was dissected away with the radio knife in an attempt to prevent extension of the growth and at the same time avoid tearing into the vessel. The apex of the mass was in the region of the right seminal vesicle. The longitudinal tear into the right wall of the bladder offered an opportunity for careful study of the interior of that viscus, which, aside from the deformity in outline, was otherwise normal in appearance. The bladder neck was normal, though pushed far up and to the left. No enlargement of the prostate was discernible and only the left ureter orifice was seen. Careful search for the right ureter orifice failed to locate it, nor could the right ureter be recognized in the right pelvis either during or after the removal of the tumor mass.

The longitudinal rent in the bladder was repaired and sutured around a Pezzar catheter and five cigarette drains were placed into various areas of the tumor bed and around the bladder. The wound was closed in layers, and the patient returned to his bed in good condition.

The postoperative course was slow but uneventful. The Pezzar catheter fell out on the 13th day and he started voiding per urethram on the 23rd day. On several occasions the suprapubic sinus reopened but it closed eventually, and he was discharged from the hospital with the wound and fistulous tract almost entirely healed on May 24th.

Because of a suspicion that the right ureter had been accidentally tied off and cut during the operation, an intravenous pyelogram was taken April 21st, three weeks after operation. It showed good function in the left kidney which was apparently normal but again no dye was visible in the right kidney. No visualization of the bladder outline could be obtained because of the leakage through the suprapubic fistula. No changes were noted in a similar study made on May 17, 1943 (Fig 1). Roentgenograms of the gastro-intestinal tract, taken May 20th, showed no intrinsic organic disease. An electrocardiogram showed a tendency to right axis deviation. Blood chemistry findings remained at the same levels throughout his hospital stay. His blood on April 19th showed 69 per cent Hb and R B C 3,300,000.

Pathologic Examination—The specimen was a large mass of firm rubbery consistency, measuring 12 x 11 x 9 cm, and weighing 579 Gm. It was of a grayish-yellow color and apparently well encapsulated. The surface showed fibrous bands which constricted portions of the mass and gave it a somewhat nodular appearance. On section, the tumor was smooth, fibrous and generally homogeneous in appearance, with two apparently fresh hemorrhages (Fig 2).

A diagnosis of granular cell myoblastoma was made after microscopic examination. Details of the histopathology are recorded at the end of the autopsy report.

Subsequent Course—Slight leakage through a pinpoint suprapubic fistula persisted until August 13, 1943 (103 days following operation) after which the cicatrix was firmly healed. Cystoscopy 89 days after operation showed a bladder capacity of 90 cc,

GRANULAR CELL MYOBLASTOMA

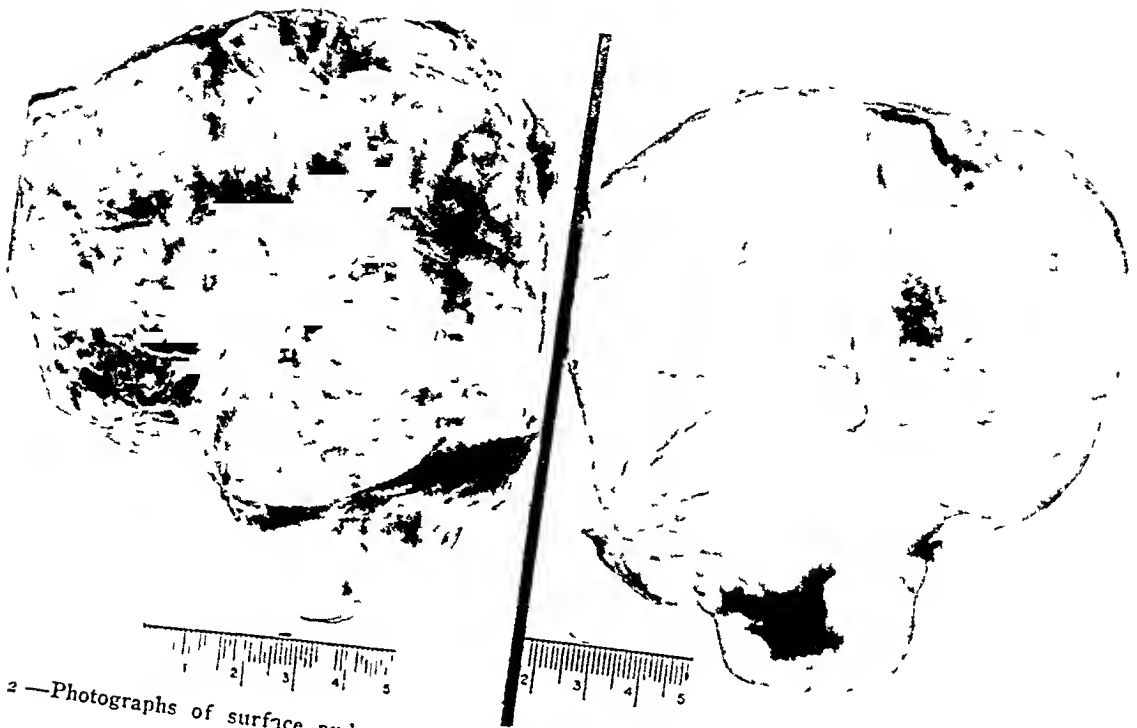


FIG 2—Photographs of surface and sagittal section of tumor removed at operation April 1, 1943



FIG 3—Roentgenogram of the 2nd lumbar vertebra taken August 29 1944—two days before death, showing advanced destruction

moderate general cystitis, considerable degree of trabeculation and congestion of the left ureteric orifice, the right ureteric orifice was not visualized. Cloudy urine and frequency continued at 104 days, but he felt well enough to return to his arduous work as pressman.

On November 24, 237 days after operation, there was slight rectal bleeding, apparently from small internal hemorrhoids. Rectal palpation at this time revealed slight thickening and fullness on the right side of the pelvis for the first time since operation. Roentgenograms and an intravenous pyelogram showed no dye and no kidney outline.



FIG 4.—Photograph of the entire urinary tract, aorta, retro peritoneal lymph nodes and recurrent tumor which formed one mass with the bladder and prostate. The right kidney is distended. The markedly dilated right ureter plunges into the pelvic tumor mass below.

on the right side, but a normal left kidney. Left kidney function was good, with slight hydronephrosis, but a fairly normal left ureter. The bladder was seen on the left side of the pelvis. No masses were palpable suprapubically. Forty-seven days later, on January 10, 1944, an indefinite mass could be felt through the rectum extending above and confluent with the right side of the prostate. He had no subjective symptoms at this time, but on February 4th he complained of slight pain in the lower abdomen. The mass felt through the rectum on the right side was larger and abdominal palpation revealed a small indefinite mass in the left iliac fossa. Palliative roentgenotherapy was given by Dr. Asa B. Friedman from February 12 to April 17, 1944. 10 x 15 cm left suprapubic and left sacral ports were used. The factors were 200 K V, 50 cm



FIG 5—Photograph of the liver riddled with metastases



FIG 6—Photograph of the spleen with countless metastatic foci

skin distance, filter 0.5 Mm Cu plus 1 Mm Al 2500 r were given through each port delivering a tumor dose of 3000 r. This produced symptomatic improvement, with disappearance of the pain. On March 30th the rectal mass felt larger and the abdominal mass slightly smaller.

By May 5th, however, the pain returned in the left flank and grew increasingly severe. He was readmitted to the Adelphi Hospital, June 17, 1944, with the idea of removing the recurrent pelvic tumor, which at this time seemed more prominent in the left iliac region than on the right side. Two days later, a roentgenogram of the spine

showed some destruction of the 2nd lumbar vertebra, which was interpreted by Dr Friedman as a metastatic lesion. Because of this finding, any further operative procedure in the pelvis was deemed futile. The vertebral destruction became progressively greater until the end (Fig 3).

Although his general condition was quite good at this time, he soon began a gradual decline. Pain was kept fairly well under control by roentgenotherapy of the vertebra, cobra venom and later various narcotics. His inguinal nodes became enlarged and, on July 25th, two of them were removed and showed metastases. Toward the end, emaciation and cachexia became extreme and he finally died August 31, 1944, 17 months after the first operation.



FIG 7—Photograph of the dome of the skull with metastases in the frontal area

AUTOPSY—Dr D. M. Grayzel. The following pertinent findings are taken from his report:

There was a large recurrent tumor mass in the pelvis which extended upward to the second lumbar vertebral body posteriorly and to within 5 cm. of the umbilicus anteriorly. It encased the urinary bladder which had only a small cavity and the bladder wall seemed to be composed of tumor tissue. Both ureters plunged into the tumor mass and were lost within its substance. The sigmoid was displaced by the tumor but apparently was not involved by it. The right kidney was purple-brown, cystic, and its pelvis was distended. The right ureter was dilated up to a diameter of 3 cm. and kinked in several places. The left kidney was reddish-brown and did not show gross evidences of disease. The retroperitoneal chain of lymph nodes were enlarged by tumor all the way up to the diaphragm (Fig 4). Above it the esophageal and tracheobronchial nodes and the nodes on the superior surface of the pericardium also seemed involved. The enlarged iliac nodes were continuous with much enlarged inguinal nodes on both sides. The liver weighed 1250 Gm., and extended 4 cm. below the xiphoid process. It was studded throughout with nodules averaging 3 mm. in diameter, some of which were confluent (Fig 5). The spleen weighed 720 grams and was

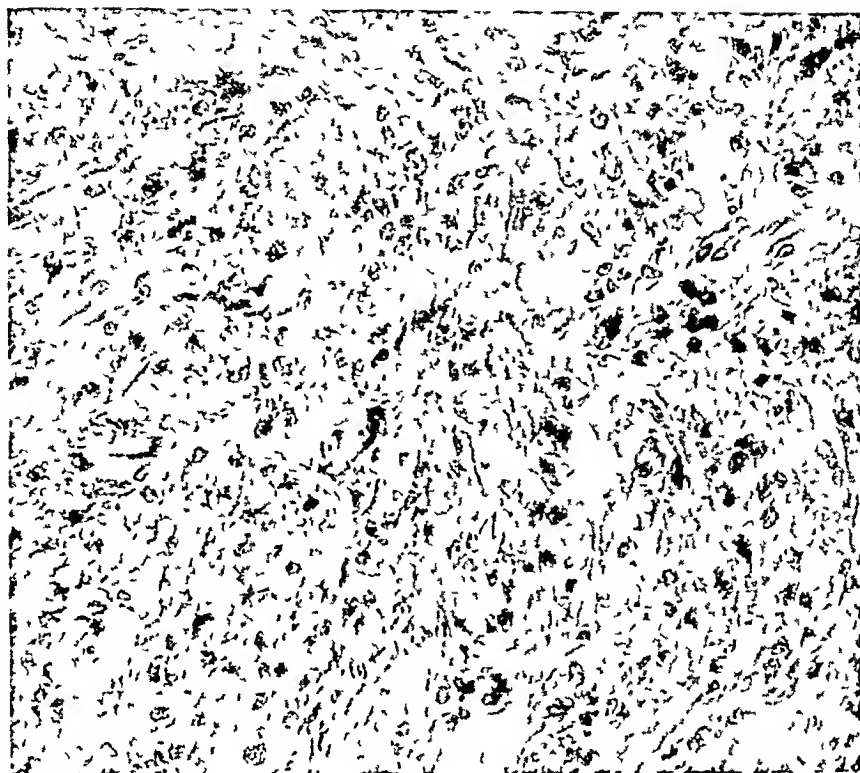


FIG 8—Photomicrograph of the primary tumor showing the arrangement of the cells and their relative shape and size

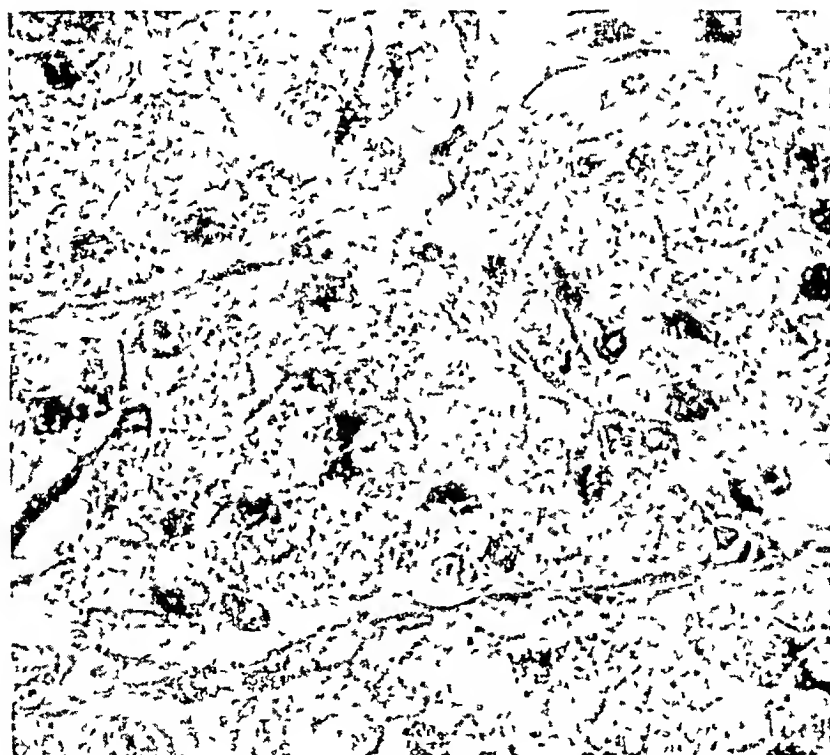


FIG 9—Photomicrograph showing details of the cells of the primary tumor and the characteristic granular cytoplasm ($\times 600$)

speckled throughout with fine yellow nodules, confluent in some areas (Fig 6) The left lung weighed 190 Gm and the right 250 Gm At the base of the right lung was a 9-Mm tumor nodule just beneath the pleura The body of the second lumbar vertebra was soft and yellow-gray, and the tumor was adherent to it Metastatic tumor in the frontal bones formed bony nodules, up to 3 cm in diameter, which could be seen and felt beneath the scalp (Fig 7) The rest of the viscera including the brain showed no evidence of metastases

Anatomic Diagnoses Tumor of urinary bladder (granular myoblastoma?) involving prostate gland, liver, spleen, lymph nodes, right lung, pericardium, skull, vertebra, peritoneum and pelvic tissues, right hydronephrosis and hydroureter, bilateral hydrothorax, hydropericardium, emaciation, decubitus ulcers and deformity of left foot

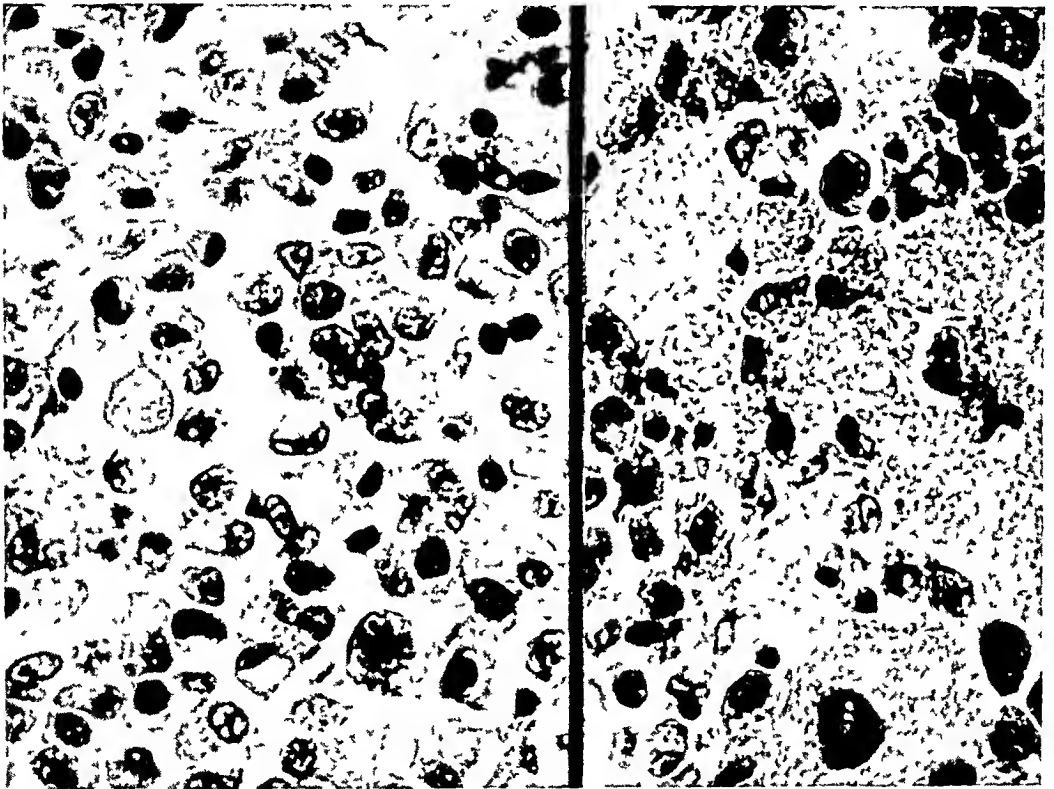


FIG 10—Photomicrograph of the tumor at autopsy At the right a detail from the recurrent mass showing large granular cells like those in the primary tumor mingled with much smaller cells At the left, small cells characteristic of the final malignant phase of the tumor They show lack of cohesion and a tendency in some to form chondriosomes ($\times 600$)

Microscopic Examination This, in general, confirmed the provisional diagnoses The bladder wall was completely replaced by tumor up to the mucosa Metastases were present in the second lumbar vertebra and frontal bone, the liver, spleen and all lymph nodes sectioned Not only was the nodule in the right lung composed of tumor cells but all sections made from the lungs contained tiny foci

The *primary tumor* is made up of cords of large, irregularly rounded and plump elongated cells with relatively small nuclei and voluminous cell bodies filled with fine acidophilic granules No longitudinal or cross striations are observed No mitoses are found but some of the larger cells have more than one nucleus and there is some variation in the relative size of the nuclei The cords of cells are separated by slender strands of connective tissue (Figs 8 and 9)

Recurrent Tumor and Metastases In a few places, notably in the local recurrent tumor mass and the lung metastases, cells resembling those in the primary tumor are

encountered (Fig 10) but for the most part the tumor cells have a different appearance. The majority are very much smaller, more definitely rounded, and they appear as distinct units instead of being in cohesive cords. The nuclei are relatively much larger, more hyperchromatic and the cytoplasm proportionately greatly reduced in amount. No mitoses are found. In most of the cells the granular habit of the cytoplasm is maintained but occasionally there seems to be some chondriosome formation (Fig 10). In none of the many sections prepared were any definite cross striations or longitudinal fibers seen. It must be remarked, however, that the tissue was fixed in formalin and no reliable preparations with Haidenham's hematoxylin or phosphotungstic acid could be made.

COMMENT—There was some question in our minds as to the exact site of origin of this tumor because at the first operation the major portion of the growth was outside of the bladder. However, its only intimate attachment was to the bladder wall and it would seem more probable that its origin was from this structure than from the retroperitoneal tissues outside of it.

The histologic features of the primary tumor compel us to classify it as an example of Abrikossoff's third group of myoblastic myomas or granular cell myoblastomas, as we prefer to call them. We have been unable to find any reports of this tumor form arising either in the bladder or in the retroperitoneal tissues. These granular cell myoblastomas are almost certainly of rhabdomyoblastic origin, as was originally pointed out by Abrikossoff on histologic grounds and confirmed by the, as yet unpublished, observations on tissue cultures by Dr. Margaret Murray, of the Laboratory of Surgical Pathology of Columbia University. The suggestion of chondriosome formation in some of the metastatic tumor cells may also be regarded as confirmatory evidence.

It need not be any cause for surprise that an embryonal striated muscle cell tumor should arise in the bladder for there are a number of cases of rhabdomyoma and rhabdomyosarcoma of that organ on record. Montpellier, in 1929, found records of 12 cases. Ten years later, Uhlmann, Grossman and Calvin found seven more, and we have found at least seven other cases not included in those two groups (Janū and Stolz, 1932, Bailey, 1934, Planque, 1937, Hirsch and Brown, 1938, Vermooten, 1939, and Hunt, 1943, two cases). All of these tumors were composed of more or less differentiated rhabdomyoblasts usually with cross striations and none had the granular cells characterizing this tumor. Most of them occurred in children and displayed their malignancy by rapid infiltrative local growth. Metastases were very uncommon.

But perhaps the most important observation here recorded is the fact that one of these granular cell myoblastomas has behaved like a malignant tumor and metastasized. So far as our information goes, this is the first proved case to have exhibited this phenomenon among 50 cases recorded in the Laboratory of Surgical Pathology of Columbia University, and nearly 100 other reported cases. It will, therefore, no longer be possible to regard the granular cell myoblastoma with equanimity as an entirely benign neoplasm which never metastasizes. On the other hand, such an event must be extremely uncommon so that usually it need not be anticipated.

SUMMARY

A malignant granular cell myoblastoma is reported which arose probably in the urinary bladder, recurred following excision, and caused death with metastases 17 months after operation. The primary growth is identified as an example of Abrikossoff's third group of myoblastic myomas. As such, it is believed to be the first example of its kind to have developed in the bladder and also the first record of such a tumor to metastasize and cause death.

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THE TREATMENT OF ACTINOMYCOSIS WITH PENICILLIN

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WITHIN THE PAST YEAR (1943-1944) six cases of actinomycosis have been treated with penicillin at the Bushnell General Hospital. All of these cases were under the supervision of one of us (J M W), and it is upon the observations and study of these cases that this paper is based.

During the past 18 months we have been interested in seven cases of actinomycosis admitted to our wards. These cases were proven actinomycotic infections by the finding of the ray fungus both macroscopically and microscopically. Most of these cases had received various other forms of therapy, including roentgenotherapy, potassium iodide and sulfa therapy. However, we felt that in the large percentage of these cases adequate sulfa therapy had not been given. It was our plan to treat five cases with penicillin therapy which was done, and then to treat two cases with adequate sulfa therapy alone. In the last group one of the cases was a success and the other case must be considered a definite failure as a recurrence, with positive drainage, took place four months later while under sulfa therapy. This one case is included in the present series as a successful result of penicillin therapy.

Herrell¹ March 4, 1944 reported four cases of actinomycosis treated with penicillin at the Mayo Clinic, with two failures. He does not state the amount of penicillin used or the length of time that penicillin was administered. It is our contention, from our own experience, that the treatment of actinomycosis with penicillin should be a prolonged one and that surgery, when feasible, should be employed in conjunction with this form of therapy.

"Actinomycosis is an infectious granulomatous disease characterized by the destruction of tissue, suppuration, and an overgrowth of fibrous tissue."² This to us is an excellent description of the disease, and one immediately becomes aware of the chronicity of the disease and why the morbidity may be a prolonged one. Meleney,³ in a recent article, in discussing drug therapy in infectious disease, lays great stress on the difference between medical and surgical infections and the pathologic characteristics which differentiate them. This is a fundamental article and well illustrates the difficulties encountered in treating actinomycosis with any drug. It is our feeling that even though the drug is extremely potent and may be lethal to the *Actinomyces*, that anyone who expects to cure a chronic actinomycotic infection in a few days with any form of drug therapy is going to be disappointed.

In September, 1942, Waksman and Woodruff⁴ reported that penicillin had a definite bacteriostatic effect on the *Actinomyces*. Since that time several other investigators have corroborated these findings. We found great difficulty in growing these organisms, due principally to the fact that the *Actinomyces* are micro-aerophilic and we were unable to get the correct

environment for growth. Due to these findings and because of the beneficial effect of other bacteriostatic agents, notably the sulfonamides⁵ on actinomycosis, we started penicillin therapy on July 4, 1943, in the clinical treatment of actinomycosis.

The six cases of actinomycosis will be broken down into three subgroups in order to illustrate more adequately the disease process and the problems of therapy.

- Group I Cases with only soft tissue involvement (two cases)
- Group II Cases with bone involvement as well as soft tissue involvement (three cases)
- Group III Cases with generalized systemic involvement (one case)

GROUP I

Case 1—White, male, age 28, born in Missouri. Patient's past history was non-contributory. In July, 1942, he had a left lower third molar tooth extracted. Two weeks later he developed swelling, pain and tenderness in the left inframandibular region which progressed, and, in September, 1942, an incision and drainage in this area was carried out. On November 1, 1942, he developed pain, swelling and tenderness in the left temporal region and, December 13, 1942, he was transferred to the Bushnell General Hospital, with a large fluctuant abscess in the left temporal region and an indurated tender area, with fluctuation in the inframandibular region. Roentgenograms showed no bone involvement.

Incision and drainage of the left temporal region and of the inframandibular region was carried out December 20, 1942. The diagnosis of actinomycosis was established grossly and microscopically. The wound continued to drain and he was treated with potassium iodide, ten drops t i d, from February 1, 1943, through February 24, 1943. He also received roentgenotherapy in February and March of 1943, 800 R units. During this time there was no improvement.

On April 5, 1943, sulfadiazine was started and carried out for two months for a total of 240 Gm. Under sulfadiazine therapy there was marked improvement. Both areas healed and there remained little or no residual induration.

He was allowed to go home at this time on a furlough, and while at home had a definite recurrence, with swelling and induration in the inframandibular region. On July 4, 1943, ray fungi were again demonstrated in the drainage from the inframandibular region and the patient was admitted for penicillin therapy. He received 15,000 units, q 3h, intravenously, for a total of 2,794,000 units for three weeks, with marked improvement and subsidence of all swelling. He was then sent to the Rehabilitation Camp, where he had a definite recurrence with positive drainage.

He was retreated from September 16, 1943, until October 8, 1943, with penicillin, 25,000 units, q 3h, intramuscularly, for a total of 4,300,000 units. Again, he showed marked improvement, but even at the conclusion of therapy there remained a small weeping area in the inframandibular region. Scar tissue and underlying fibrotic tissue was then excised and the wound closed. At operation there was no evidence of supuration. The pathologic diagnosis of chronic, inflammatory tissue from the left inframandibular region was made. The wound healed *per primam* and remained soft, with no evidence of induration.

He was discharged to duty on January 21, 1944. Recent follow-up by letter in April, 1944, states that he has remained well with no evidence of infection.

COMMENTS This patient showed an excellent response to sulfadiazine therapy initially, and it is our feeling that if sulfadiazine therapy had been

continued he might not have had a recurrence. Secondly. This patient was the first that we treated with penicillin therapy and it is obvious that three weeks were not sufficient, as evidenced by a definite recurrence. Also, it should be noted that at this time we were giving penicillin intravenously while in the second course of therapy he received the drug intramuscularly. There is little doubt that the intramuscular use is preferable to the repeated intravenous method. Lastly. It should be noted that even at the conclusion of penicillin therapy a small weeping area in the neck remained which responded satisfactorily to surgical excision of scar tissue. If the patient were to be treated at the present time we would carry out early excision of scar and fibrous tissue while under penicillin therapy.



FIG 1



FIG 2

FIG 1—Group 1, Case 2 (7-24 43). Marked cellulitis of left inframandibular region, before penicillin
FIG 2—Group 1, Case 2 (9 7 43). Six weeks later, at conclusion of penicillin therapy

Case 2—White, male, age 33, born in Minnesota. Past history was noncontributory. He had a third right lower molar tooth extracted on March 10, 1943. On April 20, 1943, he noticed a hard swelling just below the right mandible. This area increased in size and was moderately tender and he was hospitalized on April 30, 1943. On May 10, 1943, R-15 was extracted, and on May 22, 1943, external incision and drainage was carried out. On June 21, 1943, *Actinomyces* were recovered from the drainage. The patient received potassium iodide from May 13, 1943, until July 1, 1943, with an average of 100 drops a day with no improvement. On July 20, 1943, he was transferred to Bushnell General Hospital. Examination at this time revealed the whole right side of the neck below the mandible indurated and tender, with fluctuation in four separate areas (Fig 1). There was moderate drainage which contained sulphur granules. Roentgenograms were negative for bone involvement. On July 25, 1943, penicillin therapy

was instituted, 15,000 units, I V, q 3h, for a total of 43 days, with a total dose of 5,040,000 units

Three weeks after treatment had been instituted the neck showed marked improvement but there still remained an area of fluctuation. Treatment was continued for three more weeks, and this area subsided completely. At the conclusion of treatment on September 6, 1943, the entire neck was soft and pliable with no areas of induration or tenderness (Fig 2). He was observed for three months and then discharged back to duty January 11, 1944.



FIG 3a



FIG 3b

FIG 3—Group II, Case 1 (9 21 43) Showing bone involvement of right mandible

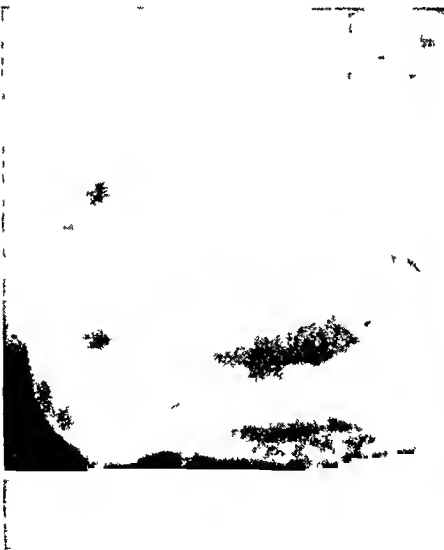


FIG 4a



FIG 4b

FIG 4—Group II, Case 1 (4 22 44) Roentgenographic evidence of bone regeneration, with subsidence of infection

COMMENTS This patient had a marked infection which was, however, limited only to the soft tissues in the maxillofacial region. It is of interest

that at the end of three weeks the disease process had not completely cleared and it was necessary to continue therapy for three additional weeks

GROUP II

Case 1—White male age 33, born in Idaho. Patient's past history was irrelevant. On July 6, 1943, he had R-10 extracted because of pain. On July 8, 1943, he developed swelling on the right side of the jaw, and on July 9, 1943, he was unable to open his mouth. The patient was treated with sulfadiazine from July 9, 1943, until September 2, 1943. He received five courses of sulfadiazine, 1 Gm q 4h, with a total of 210 Gm. Under this regimen there was no improvement, and the diagnosis of osteomyelitis of the right mandible was made. On September 2, 1943, he was transferred to Bushnell General Hospital.

Examination here revealed a chronic cellulitis of the soft tissues overlying the lower third of the right mandible. Roentgenograms revealed bone involvement and several vacuoles were present in the right mandible, the largest of these measuring 1 x 1.4 cm (Fig 3 A and B). On September 23, 1943, a small sequestrum in the apex of the first molar tooth was extracted through the floor of the mouth. Following this the patient was treated with large doses of sulfadiazine, 1 Gm q 4h, for a total of 168 Gm and also 200 R units of roentgenray to the indurated area. However, he failed to improve, and on October 20, 1943, there was definite fluctuation just below the right mandible and a small incision was made. Sulphur granules were found and the diagnosis of actinomycosis was established.

On October 20, 1943, penicillin therapy was started, 25,000 units, IM, q 3h, and this was continued until October 29, 1943, when the dosage was reduced to 15,000 units IM, q 3h, which was continued until November 11, 1943, a total of 3,360,000 units. Under penicillin therapy there was a dramatic response. At the start of treatment there was marked trismus, the patient being able to open his mouth only one centimeter, and there was marked cellulitis. At the end of ten days the cellulitis had completely disappeared, and at the end of two weeks he was able to open his mouth completely.

On November 23, 1943, 12 days after penicillin therapy had been discontinued, he developed swelling over the right mandible and roentgenograms at this time showed evidence of infection at the bases of most of the teeth. It was decided that all teeth should be extracted. Because of the cellulitis about the right mandible and also because of the previous occurrence of actinomycosis following tooth extraction, it was decided to treat the patient with penicillin while his teeth were being extracted. He was treated with penicillin from November 25, 1943, until December 22, 1943, with a total of 6,300,000 units. During this time both the upper and lower teeth were extracted except for two which were left *in situ* in order to anchor dental plates.

This patient had an uneventful course following teeth extraction. At no time were we able to note any drainage. He was followed for a period of seven months, with no recurrence. It is interesting to note that the bony lesions had healed completely by the time of discharge (Fig 4 A and B).

COMMENTS This case is interesting for several reasons. The patient received a total of 378 Gm of sulfadiazine previous to penicillin therapy without benefit. It is also interesting that the patient had a definite swelling following the first course of penicillin therapy. However, this swelling was not in the region of the original cellulitis but approximately three inches away. Whether this cellulitis was due to actinomycosis cannot be determined. It should be noted that following extraction of teeth plus penicillin therapy, the bony lesions in the right mandible cleared.

Case 2—White, male, age 23, born in Kansas City, Mo., first noticed tenderness

and swelling in the region of the left temporomandibular joint on May 24, 1943. He went to the Dental Clinic at a Station Hospital in California, and had four teeth filled. Four days later there was marked pain in the left side of the neck and jaw, and roentgenograms revealed an impacted left upper third molar, which was extracted. Twenty-four hours after operation pain and swelling increased, and there was fixation of the lower jaw, in occlusion. He was treated with sulfathiazole, 1 Gm qid from June 12, 1943, until June 29, 1943. He was then transferred to a General Hospital where he was given roentgenotherapy for three days, 300 R units daily, for a total of 900 R units. On July 2, 1943, an incision in the inframandibular region was made and sulfanilamide was placed in the wound. Drainage positive for *Actinomyces* was obtained.

On July 23, 1943, he was transferred to Bushnell General Hospital. On examination, there was marked cellulitis of the supramandibular region and of the inframandibular region, with a chronic suppurative wound in the inframandibular region. There was marked trismus, he being able to open his mouth only one centimeter. Roentgenograms of the left mandible at this time showed periostitis of the ramus of the left mandible and an abscess in the middle third of the left ramus. The drainage from the left inframandibular wound was positive for ray fungi. On July 25, 1943, the patient was admitted to the penicillin ward with a temperature of 99.8° F. Laboratory work-up was within normal limits. Penicillin therapy was started this day, 15,000 units, IV, every three hours. He was treated for six weeks with this dosage, and the inframandibular region cleared but the supramandibular region remained markedly indurated. Dosage was then increased to 25,000 units, IM, for two weeks, and the supramandibular region softened completely during this time. Trismus had disappeared at the end of six weeks. This patient received a total of 7,845,000 units of penicillin. Approximately three months after penicillin was discontinued he developed a small firm mass in the region of the submaxillary gland on the left side, and he was treated with sulfadiazine for three months, with clearing of this region.

COMMENTS There are several interesting features in this case. This patient had extensive actinomycosis, with a marked overgrowth of fibrous tissue as well as bone involvement. He responded well to penicillin therapy, but only after a long course of treatment. He would undoubtedly have done better if surgery had been carried out while under penicillin therapy, with excision of the fibrous tissue. It is interesting to note that approximately three to four months after penicillin therapy had been discontinued he developed a firm nodule in the region of the submaxillary gland which subsided under sulfadiazine therapy. Roentgenograms taken in May, 1944, show a clearing of the periostitis, but there still remains a small area with decreased density in the body of the left mandible, which is apparently filling in satisfactorily.

Case 3—White, male, age 18, born in St. Louis, Mo. On December 12, 1943, he developed sore, swollen gums at the base of the incisor teeth of the lower jaw. On December 19, 1943, there was a fluctuant mass noted in the mental region. Incision and drainage was carried out, and drainage was positive for ray fungi. Roentgenograms taken on December 22, 1943, showed a punched-out area in the lower third of the right mandible. Following this he was placed immediately on sulfadiazine therapy, which was continued for four months. Treatment was started with sulfadiazine Gm 1 q4h for two weeks and then cut down to Gm 1 qid, and then Gm 1 tid. The sulfadiazine blood level was maintained between 4 and 8 mg per cent. Under this therapy he improved, but on April 16, 1944, an area in the mental region broke down at the site of the previous incision, and drainage was again positive for ray fungi. On April 20, 1944,

he was admitted to the penicillin ward and penicillin was started 25,000 units, IM, q 3h, which was continued until May 20, 1944, a total of 5,975,000 units. He showed immediate and marked improvement under penicillin therapy but there remained a hard indurated area in the mental region. On May 4, 1944, 14 days after penicillin therapy had been started, a transverse incision just below the mandible was made and scar and granulation tissue was excised. The bony lesion in the mandible was curetted at the same time. The wound was closed with interrupted silk sutures, and he had an uneventful postoperative course. All signs of induration disappeared at the end of seven days, and penicillin was discontinued on May 20, 1944.

COMMENTS This patient had very little cellulitis but had marked fibrosis of the soft tissue, with a good-sized defect in the mandible. Sulfonamide therapy was a failure in this case but there was a good response to penicillin plus surgery. It is worth observing that surgery was carried out two weeks after penicillin therapy had been started, with excision of dense, fibrous and granulation tissue, and that the wound was closed and healed *per primam*. Although this case has only been followed for a period of three weeks after the discontinuance of penicillin, the skin at this time is soft and pliable, with no evidence of induration. Follow-up has not been long enough, but the patient appears clinically cured.

GROUP III

Case 1—White, male, age 50, born in Los Angeles, Calif. He developed dyspnea, followed by cough, increased sputum and hemoptysis in October, 1942, in Hawaii. He was hospitalized. No definite diagnosis was established but he was placed on potassium iodide, 30 drops t i d and sulfathiazole, Gm 1 q i d for one month in November, 1942. He was then transferred to a General Hospital in December, 1942, where no definite diagnosis was established, but the diagnosis of a possible malignancy in the left upper lobe was entertained (Fig 5). In February, 1943, he was transferred to another General Hospital and while enroute he developed pain, tenderness and swelling just below the right knee joint. This broke down in the later part of February, and a short time later the diagnosis of actinomycosis was established by finding ray fungi in the drainage from this area. He was treated with sulfathiazole, Gm 1 q 4h, for 15 days in February. He continued to go downhill, with marked weight loss, increase in sputum and pain in the left chest. He was treated with sulfadiazine, Gm 1 q i d for three weeks in April, 1943. About this time infiltration about the right diaphragm was noted.

On July 15, 1943, he complained of severe pain in the back and this became progressively worse. On August 1, 1943, a right subhepatic abscess was incised and drained. Following incision and drainage of the abscess he failed to show improvement. His general condition by this time had become critical. He had lost approximately 70 pounds in weight, and was taking either morphine, Gm 0.015 or diluadid, Gm 0.004 every four hours. On August 24, 1943, he was transferred to Bushnell General Hospital and was admitted on the 25th. Examination at this time revealed a chronically ill, emaciated white male, who was in a critical condition.

He complained of marked pain in the left upper and right lower chest. He was raising approximately 100 cc of thick sputum daily. Physical examination revealed dullness at the left apex, with occasional moist râles, decreased breath sounds at the right base, with moist râles on coughing. There was a draining abdominal wound which contained 6 to 8 feet of two-inch packing. The skin from the lateral and medial aspect below the right knee joint had been excised for an area of approximately 12 by 8 cm on each side but there were two draining sinus tracts, one laterally and one medially, which extended up toward the knee joint. Examination of the sputum

revealed typical sulphur granules, which were confirmed by laboratory diagnosis. The drainage from the right subhepatic area and, from just below the right knee joint showed gross and microscopic ray fungi. Temperature on admission was 100.2°F , R B C 3,100,000, hemoglobin 11 Gm, W B C 13,700, with a sedimentation rate of 37.

Roentgenograms of the chest revealed an exudative fibrotic lesion in the left apex and a similar lesion at the right base, with fixation of the right diaphragm (Fig 6)

FIG 5

FIG 6

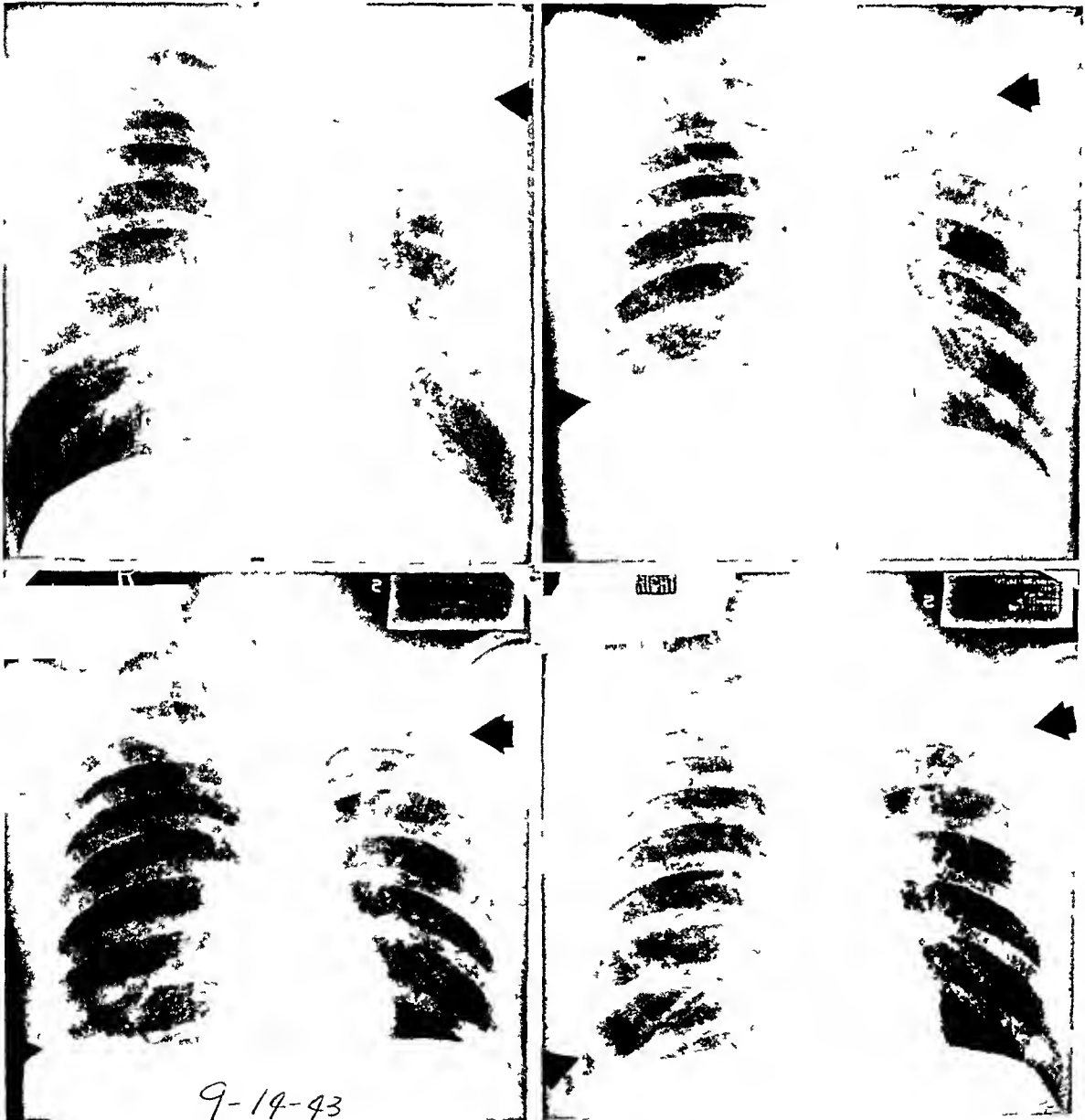


FIG 7

FIG 8

- FIG 5—Group III, Case 1 (2 2 43) Showing exudative infiltration and fibrosis of left upper lobe
 FIG 6—Group III, Case 1 (7 17 43) Showing involvement of right base, with changes similar to those of left upper lobe
 FIG 7—Group III, Case 1 (9 14 43) After three weeks of penicillin therapy. Note improvement
 FIG 8—Group III, Case 1 (11 4 43) Two weeks after termination of penicillin, showing marked clearing of exudative reaction

Roentgenograms of the right knee joint showed slight to moderate destruction of the cartilage of the medial condyle of the femur. He was started on both systemic and local penicillin. He received 15,000 units, IM, q 3h, from August 5, 1943, through August 27, 1943, and then 25,000 units August 28, 1943, through September 15, 1943, and then 15,000 units from September 16, 1943, through October 20, 1943—a total of 8,170,000 units. He was receiving local penicillin, 250 units to the cubic centimeter, into the abdominal wound and to the granulating areas below the right knee joint.

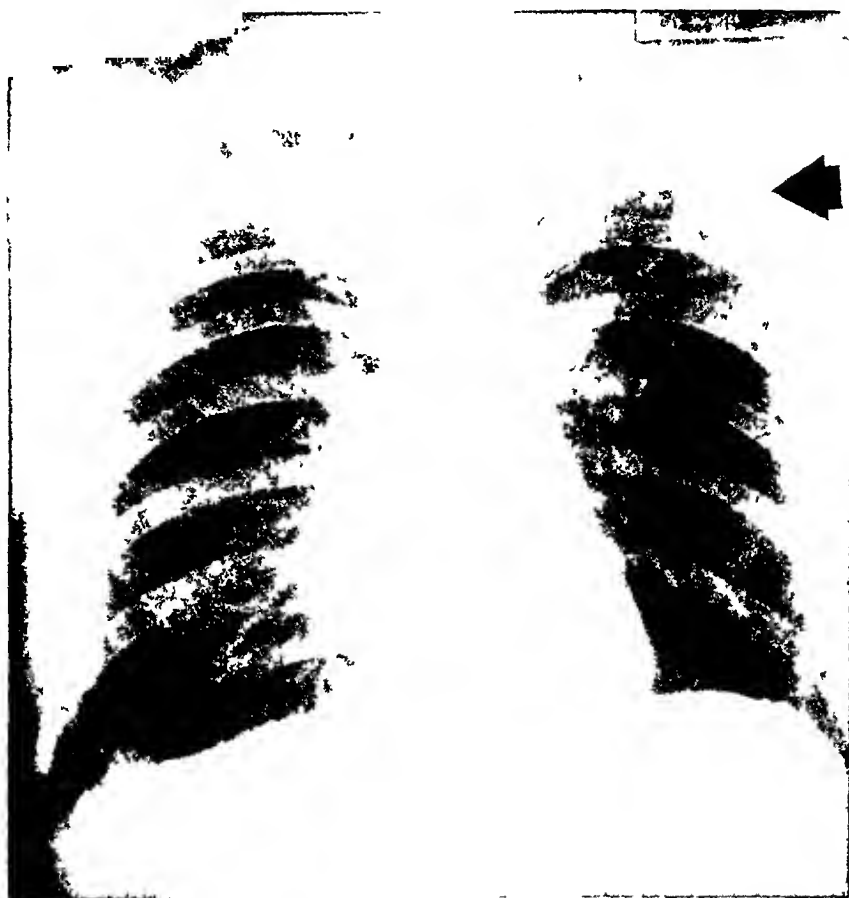


Fig 9—Group III, Case 1 (31444). Inflammatory process has resolved, only residual fibrosis remains.

There was a dramatic response to penicillin therapy. Within 24 hours it was possible to stop the narcotics. Within five days his temperature had become normal, and remained below 99° F after this. Within two weeks time he had ceased raising sputum, and all drainage from the knee joint and subhepatic area had also ceased (Fig 7). During the eight-weeks course of penicillin therapy he gained 25 pounds in weight.

One month after penicillin therapy had been instituted, roentgenograms of the cecum and ascending colon were taken. Barium enema showed definite involvement of the cecum and ascending colon. After penicillin had been discontinued he continued to improve and all wounds had healed solidly at the end of 25 months. The patient was followed until May 5, 1944, when he was retired from the Army. In February, 1944, while there was no evidence of active infection, it was decided, because of the extensive nature of the disease, that a course of sulfonamide therapy should be administered, and he received sulfadiazine, Gm 1 qid, and then Gm 1 tid for two months. At the time of discharge he had no complaints, except for moderate dyspnea on exertion and pain in damp weather in the left shoulder joint.

He had gained 63 pounds, R B C was 4,800,000, with 15.2 Gm of hemoglobin,

and W B C ranged between 6,000 and 8,000, with a normal differential Sedimentation rate was 1 to 3 millimeters Roentgenograms showed complete clearing of the process at the right base, except for a minimal amount of fibrosis The right diaphragm which had been fixed had become mobile There was still moderate fibrosis of the left upper lobe G I series and barium enema showed no organic pathology, except for a diverticulum of the duodenum An electrocardiogram was reported normal

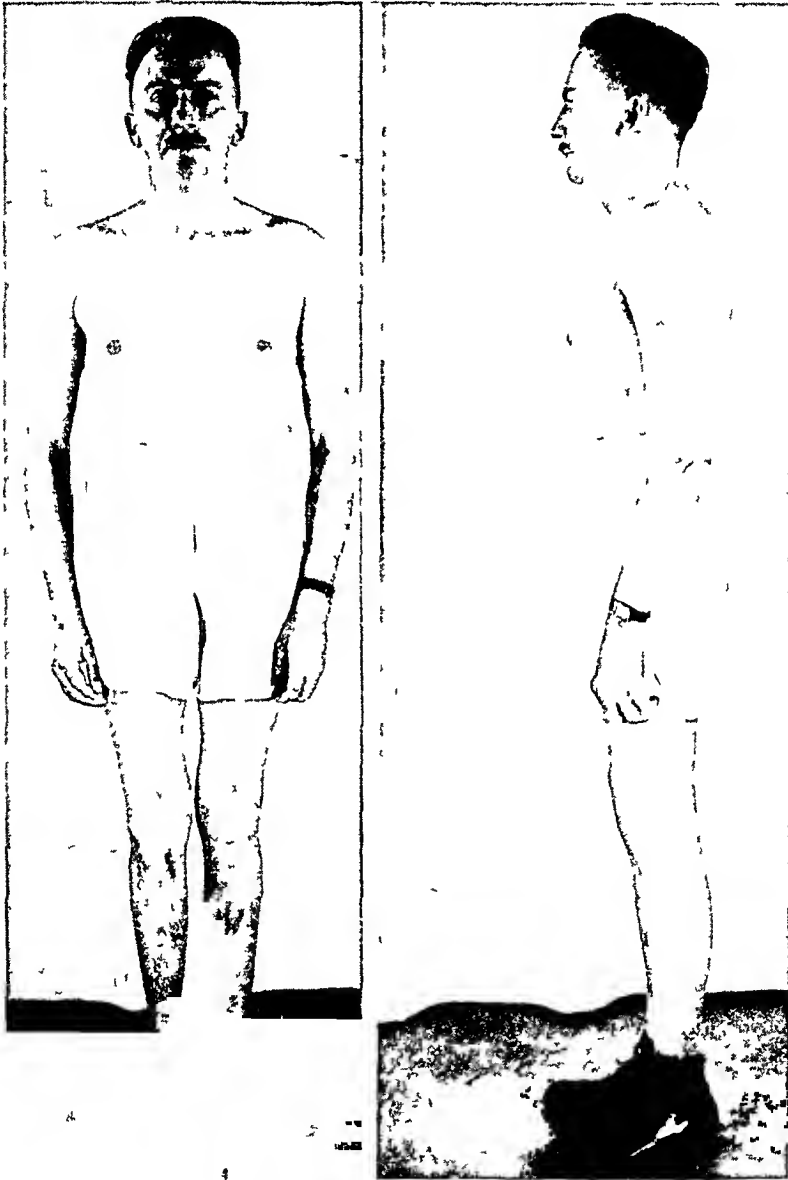


FIG 10—Group III, Case 1 (4 17 44) Showing general nutritional state at time of discharge

COMMENTS This case represents a severe, generalized actinomycotic infection, involving the left lung, right lung, right diaphragm, cecum and ascending colon, with a subhepatic abscess, and infection of the skin and underlying tissue below the right knee joint Whether the knee joint itself was involved is open to question There were two sinus tracts, one lateral and one medial, which extended up to the joint Roentgenograms showed

only roughening of the cartilage over the medial condyle of the femur. The response to penicillin was brilliant. It was almost unbelievable to see the rapid improvement of this dying man to penicillin therapy.

He was followed seven months after termination of penicillin therapy, with no evidence of recurrence. It should be noted that in February and March, 1944, he received sulfadiazine therapy. Although the patient at this time showed no evidence of infection, one of us (J. M. W.) felt that the disease process had been so extensive that sulfadiazine as a prophylactic measure should be administered. Whether this had any effect is difficult to say.

DISCUSSION—In these six cases of actinomycotic infection there are several interesting features. Only two of the cases had had a diagnosis of actinomycosis made before admission to this hospital. This is not particularly surprising, but we believe that with any chronic cellulitis, especially in the maxillofacial region, the diagnosis should be entertained, and once entertained it is usually soon established if present. However, the surgeon in charge of the case should establish the diagnosis by the finding of the sulphur granules. It then becomes his responsibility to see that these granules are promptly sent to the laboratory for examination. Frequently simply a swab of pus is sent to the laboratory for smear and culture, and the result is that the diagnosis is not made.

In not one of these cases could a history of chewing straw, *etc.*, be obtained. We thus feel in accord with Colebrook,⁶ Cope,⁷ and others, that the fungus may be harbored in the human mouth, and we believe that Henrici⁸ is correct in his assumption that the fungus may be modified to a fragmented or bacillary form in the mouth so that it is extremely difficult to identify. It also naturally follows that with trauma, such as tooth extraction or infection (gingivitis), a break in the mucous membrane plus tissue necrosis takes place and a fertile bed for the growth of a micro-aerophilic organism occurs.

As far as penicillin therapy is concerned, the six cases illustrate the fact that penicillin is an effective agent in combating the disease actinomycosis. All six cases responded well to the drug. The response of Case 1, Group III, was nothing short of miraculous. Several of these patients were treated with repeated intravenous injections of penicillin. This method has been discarded as the intramuscular route is undoubtedly superior. It should be noted, also, that surgical excision of scar and underlying fibrous and granulation tissue was undertaken in two cases. We believe that this step is a good adjunct to penicillin therapy where there is marked overgrowth of fibrous tissue. Both cases healed *per primam*. It is evident because of the nature of the disease process that penicillin must be administered for an adequate period of time. We started out with the idea of treating these cases for three weeks, but from our own experience we found that it usually required six to eight weeks.

There is little doubt that the sulfonamides are effective against this disease, and it might well be that a combination of the two drugs could be employed to advantage. Due to the fact that we were attempting to evaluate the effect

of penicillin this was not done. In two of the cases sulfadiazine was administered at a later date.

There is little doubt that today penicillin is the most effective therapeutic agent we have in the treatment of actinomycosis.

CONCLUSIONS

*1 Six cases of actinomycosis were treated with penicillin therapy, with favorable results. It is fully realized that the follow-up periods have not been adequate to establish permanent cure.

2 The treatment with penicillin must be prolonged.

3 Surgical excision should be used as an adjunct to penicillin therapy when there is marked fibrosis and scarring, which is amenable to it.

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* A severe case of actinomycosis of the inframandibular region with bone involvement has since been treated with penicillin and surgery with a favorable result.

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MEETING HELD AT HOT SPRINGS, VA.
DECEMBER 5-7, 1944

ADDRESS OF THE PRESIDENT

WHITHER ANON*

ALTON OCHSNER, M.D.

NEW ORLEANS, LA

FROM THE DEPARTMENT OF SURGERY, SCHOOL OF MEDICINE, TULANE UNIVERSITY,
AND THE OCHSNER CLINIC, NEW ORLEANS, LA

THOSE OF US who were present will not soon forget the meeting of the Southern Surgical Association in 1941, which was held only a few days after that tragic Sunday of December 7. Since that time we have all concentrated our attentions and efforts toward eliminating Nazism, Fascism, and "Rising Sunism." Now, however, with the possibility that the war may end none too quickly, we, as a medical profession, are confronted by new problems and must face new horizons.

Unfortunately, during the period of global conflict medical education has suffered materially. In order to furnish more physicians for the Armed Forces, medical schools cooperated with the Army, Navy, and Public Health Services in accelerating the medical school programs. Although every attempt was made to give courses equal to those given in peace time, generally this has not been accomplished for two reasons: first, many students became "stale" or fatigued because of the intensive training which they received, and, second, and probably more important, many of the teaching personnel volunteered for active duty which left only a skeleton staff to carry on the instruction. Although undergraduate teaching has suffered considerably, this is of relatively little consequence when compared with the almost complete interruption in graduate training. Unfortunately, the high standards which had been set and attained by the various certifying boards and approving bodies

* Address delivered before the Fifty-sixth Annual Session of the Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

had to be disregarded during the war period, because with few exceptions medical graduates enter active military service immediately after a nine months' internship and only a few are able to obtain a nine months' or possibly an eighteen months' residency. Because of this, the specialty training program which had been so carefully developed and which was operating so efficiently before war was declared collapsed completely, and for the war period there will be a very small number of specialists trained, resulting in a great decrease in the total number of especially trained physicians. In the post-war period, as quickly as demobilization is accomplished, there will be a need for a large number of places for advanced training, because not only will those physicians who in normal times would have obtained specialty training want it, but also many others will desire residencies. Many of the latter group will be stimulated to request specialty training because of the experience which they have had with specialty group practice in the service. This is evidenced by the results of the pilot survey made by the Committee on Post-War Medical Service which showed that slightly over 80 per cent of the men in service desired additional training and that over half (58.2 per cent) desired a prolonged training.¹ As the number of residencies and fellowships which were available before the outbreak of the war was insufficient to satisfy the demands at that time, it is obvious that the number of places available for specialty training will be woefully inadequate in the post-war period. It is estimated that approximately 15,000 men will desire some type of surgical training and that 10,000 will want prolonged training in surgery,¹ and since in 1943 there were only 2,584 approved surgical residencies,² it is, thus, evident that additional facilities must be made available for the training of these men. Davison³ has suggested that the number of residencies might be doubled in the post-war period in order to accommodate an increased number of trainees. Although this probably should be done in many institutions, it is not particularly desirable because it would decrease the value of a residency, particularly in the surgical specialties in which a relatively greater number of patients are required for resident training than in the medical specialties. Whereas a dozen or more graduate students can examine the same medical patient with approximately equal benefit to all, only one surgeon can operate upon a patient. Additional places for graduate training can be obtained by using facilities which have not been utilized before. There are in the United States a large number of institutions which have not been approved for residencies, but which can, should, and must be utilized in the post-war period. It is obvious that the obtaining of additional beds alone is not all that is necessary for increasing the number of suitable residencies. Of even more importance is the supervision of work done by the trainee. Unfortunately, in the past there has been supervision only in the well-controlled institutions, and generally those in which teaching has been done. There is no reason, however, why in the future outlying institutions cannot be placed under the jurisdiction of a teaching institution and be utilized for

resident training Such plans are in operation now in California under the auspices of the University of California Medical School, in Michigan under the auspices of the University of Michigan Medical School, and are contemplated in Louisiana under the auspices of Tulane University It is proposed that supervision of the trainees in the outlying institutions be done either by a full-time staff member who is supplied by and who is directly responsible to the University or by a responsible member of the staff who is appointed as the University representative in that institution These men would be responsible for and would supervise the work of the residents and would report from time to time to the University The residents should spend a certain period (probably six months) of their training in the University proper at which time they would receive training in the fundamental sciences In this way a large number of additional residencies could be made available in all branches of medicine, and yet a high standard of training could be maintained It is possible that a resident after having served several years in a university hospital might be appointed as chief resident in one of the smaller hospitals This would permit him to have considerable experience and responsibility and at the same time he could exert an excellent influence on the practice of medicine in that hospital, because he would be able to bring to the institution the methods, ideas, and ideals of the teaching hospital In order for this plan to be successful, it would be necessary to have the hearty cooperation of the staffs of the hospitals concerned, and it is possible that there might be some antagonism to the plan On the other hand, if the staff members of these hospitals would appreciate the fact that in this way, and in this way alone, would it be possible for them to attract well-trained residents, they would realize the value of the plan to the hospital, their patients, and themselves

It has been emphasized by Dean Kostmayer, of Tulane University, that in the future some provision should be made whereby it will be virtually obligatory for every physician to take postgraduate courses from time to time There is no science which is less static than medicine, and it is untenable for a physician to assume that because he has received his diploma and license to practice medicine he need no longer study and keep abreast of the times Fortunately, the need for obtaining additional graduate training from time to time is appreciated by most physicians, but, unfortunately for the public, those who need it most realize it the least and seldom, if ever, have any further training It would be extremely desirable, however, if it were necessary to renew at periodic intervals the license to practice and if such a renewal were possible only if the physician could show evidence of having received additional training

For the past decade and a half we have all heard a great deal about socialized medicine, and most of the medical profession have immediately condemned this form of practice as being detrimental to good practice and as one which would destroy medicine in general I fear that many times the arguments advanced by the profession against this form of practice have been

for personal reasons, and although self-preservation is desirable, it is less likely to be accepted as justification for the continuation of private medical practice than a less selfish one. Unfortunately, when one speaks of socialized medicine, it is usually not realized that even at the present time medicine is to a certain extent socialized. Certainly the care of the indigent patient in federal, state, or city charitable institutions is socialized medicine. The activities of the Public Health Service in its control of the communicable diseases, the medicine in the Armed Services, and that practiced in institutions for tuberculosis and mental diseases are forms of socialized medicine. Even in private practice, the frequently used plan of a sliding scale of fees is a type of socialized medicine. A total expenditure for medical care in a normal year is \$3,656,000,000, of which \$509,000,000 (16 per cent) is paid directly by the government.⁴ At the outset, therefore, we all must admit that we already have socialized medicine and have practiced it for some time.

Before one can consider intelligently the necessities, advantages, and disadvantages of proposed federal legislation to supply complete medical care to all persons, there are several questions which should be answered. Is there need for any change in medical practice in America to-day? Is medical practice adequate to meet the present requirements? Are the proponents of federal medicine justified in their claims that a change must be made? The statement has been made frequently in the past that in the United States to-day the best medicine of the world is practiced. This is undoubtedly true for indigents who can be admitted to charity institutions, particularly if these hospitals are staffed by the faculty of a medical school. This is also true for the wealthy who are able to obtain and to pay for the required medical care. However, is it possible for the masses of people who comprise the so-called white collar class to obtain adequate medical attention? According to Simons and Sinar⁵ "The first point to determine is whether there is, in the United States, any large section of the population with an income too small to meet the cost of necessary medical care. This question must never be raised among those familiar with the facts. That it is continuously raised, and the existence of such a class denied by representatives of the medical profession, is one of the principal counts and indictments of economic and social ignorance brought against those professions. There is not a single competent student of the subject who does not agree that several million of the population in this country receive incomes insufficient to purchase the fundamental necessities of life. This conclusion is indorsed by employers' organizations and trade unions, by the United States Bureau of Labor, charity workers, economists, statisticians, and sociologists of every type and attitude. It is one of the very few undisputed facts in the realm of economics. Yet, its explicit or implied denial is constantly found in writings admitted to medical and general journals." According to Buehler,⁶ in 1928, at the height of prosperity, 15 per cent of families had an annual income of less than \$1200 00, 34.8 per cent had an income from \$1200 00 to \$2000 00, 24.6 per cent an income of \$2,000 00 to

\$3,000 00, 15.7 per cent an income from \$3,000 00 to \$5,000 00, 7 per cent an income from \$5,000 00 to \$10,000 00, and only 2.9 per cent had an income of \$10,000 00 or more. Seventy-four and eight-tenths, or approximately three-fourths of all families, had an annual income of \$3,000 00 or less and half (49.8 per cent) had incomes of \$2,000 00 or less even in boom times. The average annual costs of medical care for these same groups were as follows: under \$1200 00, \$49 00, \$1200 00 to \$2000 00, \$67 00, \$2,000 00 to \$3,000 00, \$95 00, \$3,000 00 to \$5,000 00, \$138 00, \$5,000 00 to \$10,000 00, \$249 00, and \$10,000 00 or more, \$503 00. Reed⁴ showed in a study made in 1928 of the incomes of 29,000,000 families that 14 per cent of the families with an average of four and one-half persons per family had incomes of less than \$1,000 00, 30.3 per cent had an income of \$1400 00 or less, 68.1 per cent had an income of \$2500 00 or less, whereas 90.8 per cent had an income of \$5000 00 or less. There were only 9.2 per cent with family incomes of \$5,000 00, and 2.67 per cent with incomes over \$10,000 00. Over half of the families (55.3 per cent) had an income of \$2,000 00 or less. Carey,⁷ from 1935-1936 statistics, found that there were over twelve million families with annual incomes of \$1,000 00 or less and over two million with incomes of \$500 00 or less. From 1942 statistics, at which time there was considerable employment and high wages were paid, he found that there were thirteen million families with incomes of \$1500 00 or less. Carey⁷ maintains, and justly so, that the 1935-1936 statistics probably more closely approach the post-war incomes than those of 1942. It is, thus, apparent that there are many families even now, and in the post-war period there will be probably many more, who can afford to pay only a modest amount for medical care. On the other hand, it must be emphasized that a much larger quantity of money is spent on luxuries than for medical care. According to Cabot⁸ more than four times the amount spent on medical care is spent for "passenger automobiles, noncommercial use of gasoline, tobacco, candy, cosmetics, soft drinks, toys, jewelry, and amusements." According to Reed⁴ "The amount spent each year for tobacco alone is not quite the total gross income of all physicians, the amount spent on candy is more than twice that expended on civilian hospitals, the amount spent for cosmetics is about twice the expenditures for nurses."

Unfortunately, with the advance of medical sciences and with the increase in specialization which has become necessary since medicine has gotten so complicated it has become impossible for one to familiarize himself with all branches. Diagnosis has become more complicated and more difficult, and a more prolonged and elaborate training of the physician is essential. Whereas our predecessors made a diagnosis by looking at the tongue, counting the pulse, and recording the temperature, and they were correct in a large number of instances, at the present time such a cursory investigation could not and would not be accepted. I am perfectly willing to admit that the general practitioner of fifty years ago could tell more on a single visit

by the use of his own special senses and without elaborate diagnostic instruments than the specialist of to-day, and it is probable that the modern physician does not develop the faculty for depending upon his own resources and relies upon more complicated laboratory procedures. On the other hand, was the practitioner of fifty years ago able to make a diagnosis of bronchiogenic carcinoma, adenoma of the parathyroid, or osteoid osteoma, to say nothing about the many other diseases which were unknown at that time and which can be diagnosed only by laboratory examinations, many of which are complicated and prolonged? In order to perform these complicated laboratory examinations it is necessary to have expensive, elaborate equipment in addition to highly trained physicians and technicians. The increased cost of medical care at the present time is attributable to several factors: (1) the greater expenditure necessary to obtain a medical training, (2) the need for frequent consultations with especially trained physicians because of the great advances in medicine, and (3) the necessity of complicated laboratory examinations. It is my belief that the last factor is probably the most important of all in increasing medical costs, because there is no physician who would not treat a patient no matter how poor he may be and who would not give his services either without cost or for that which he can pay. On the other hand, decrease in the fees for complicated laboratory examinations has not been possible, and this, probably more than anything else, has been responsible for not obtaining the examinations needed in many cases. I would not care to leave the impression that complicated laboratory examinations are undesirable. In fact, without some, many of the modern more common diagnoses would not be possible. On the other hand, because of the cost of the complicated laboratory work, a physician is tempted to refrain from using them in order to save the patient with a moderate income the additional expense. Because of this, his diagnostic acumen is decreased and without a correct diagnosis, therapeutics is likely to be symptomatic, unscientific, and ineffectual. In this way, and in this way alone, is the medicine of to-day not the type it should be for a large number of persons who cannot afford such expensive examinations. That the increase in medical care is not because the physician charges too much is evidenced by the estimated income of physicians as determined in 1929, which was the year of high prosperity.⁹ Of all private practitioners, one-half had annual net incomes of \$4,000.00 or less. The other half of all physicians had an average net income of \$5,700.00. This includes all physicians: general practitioners, partial and complete specialists. It is estimated that in 1929, 33 per cent of the physicians and 22 per cent of the dentists had inadequate incomes, taking \$2500.00 as the net income which would be adequate. In 1932, at which time there was a definite decline in the income of physicians (an estimated 40 per cent between 1929 and 1932), the average net income of all physicians in private practice was \$3,450.00.⁹

The amount of money spent for medical care annually is about three and two-thirds billions of dollars, which represents approximately 4 per cent

of the income of the entire population. Approximately 14 per cent of this amount is provided by tax funds (federal, state, and local), philanthropies provide 5 per cent, industry, 2 per cent, the remaining 79 per cent is paid by private individuals.⁹ The cost of medical care, including hospitalization, medicine, and physicians' fees, is considerable, but it is only a portion of the cost of sickness. Generally, the income of the wage earner decreases or stops entirely during an illness, and this is even more of a financial burden than the cost of medical treatment. There are in each year about eight recognized illnesses among each ten persons, seven for each ten males and nine for each ten females.⁹ Because of this, it becomes increasingly more important for medical practice to emphasize prophylaxis as well as treatment because if the individual can be kept well and if sickness can be prevented, the cost will be materially less because his earning capacity will not be interfered with. It has been estimated by Falk⁹ that about 500 cases of disabling illness will occur in an ordinary year among each 1,000 persons of the population. Among those occupied in gainful occupations between the ages of fifteen and sixty-five, about 28 per cent will have one or more disabling illnesses during a year, 15 per cent will be disabled for eight days or less, 10 per cent will be disabled for nine to forty-five days, and from 2 to 25 per cent from forty-five to three hundred and sixty-five days.

These figures indicate that the economics of medicine as practiced today can be and are hardships to a large number of people and that some change in medical practice is necessary. The problem of meeting the costs of medical care would not be so difficult if one were able to anticipate an illness at any particular time and budget for it. Fortunately for those who remain well, sickness does not occur with regularity. One may go several or more years with no illness, but finally have several illnesses within a short time. According to Falk,⁹ the annual incidence of illness in 1,000,000 persons is as follows: 470,000 will suffer no recognized illness, 320,000 will be sick only once, 140,000 will be sick twice, 50,000 will be sick three times, and 20,000 will be sick four times or more. It is during the years that illness occurs or multiple illnesses occur that the burden is thrown upon those who have modest incomes.

The present difficulty is not primarily the fault of the medical profession because, as shown by the average income of physicians, the high cost of medical care is not due to excessive earnings by the profession. Although we of the profession are not directly responsible for the hardship resulting from increased medical costs, we should not deny that a need for a constructive plan exists and should actively support or institute such a plan. The proponents of federal medicine have justification in their arguments that a change in medical practice is necessary. It is my belief that organized medicine has been derelict in not assuming its proper leadership by not fostering a national plan for medical care. We should accept the admonition of the disciple Luke: "Physician, heal thyself" (Luke 4:23). No longer should we as a profession deny that a change is necessary and to continue

arguing that any plan which might be introduced by the Federal Government is undesirable because it would destroy medical practice will continue to bring discredit upon the profession because of apparently selfish motives. On the other hand, unless the medical profession offers a plan which is constructive and which will correct the now existing deficiencies, there is not only the possibility but also the likelihood that some type of Federal Medicine will be adopted. Therefore, we physicians should, in the words of Milton "Awake, arise, or be forever fallen" (*Paradise Lost*). Since socialization of medicine already exists and since it is evident that the proponents of Federal medicine have justification in their arguments that a change in medical practice is necessary, the question naturally arises whether there should be federalization of medicine, as proposed in the Murray-Wagner-Dingell Bill or not. Because of the inability of a large class of individuals to pay for adequate medical care, it is obvious that some plan must be instituted which will provide adequate care for all individuals. Can this be accomplished without federalization of medicine with its bureaucracies, wastefulness, and inefficiencies? Is it possible to permit budgeting for illness, because illness cannot ordinarily be budgeted in the way that other expenditures can and can this be done effectively or efficiently? The budgeting for illness could be accomplished by means of some form of prepayment plan for medical care. At the present time, there are in force in the United States a number of such plans, but which unfortunately are limited to certain states. The value of budgeting for illness is exemplified by the benefits which have been derived from the Blue Cross Plan which permits prepayment for hospitalization. Before the introduction of this plan, which at the present time has approximately 16,000,000 subscribers, the high cost of hospitalization was prohibitive to a great many persons with moderate incomes. Now with the prepayment plan for hospitalization this part of medical care no longer represents a hardship. Although the Blue Cross Plan does not apply to medical care aside from hospitalization, it has been valuable in relieving medical costs, because by being relieved of the burden of paying the hospital, one is better able to pay his physician. In this way the physician has also profited. It is probable that the most practical plan would be one which would not cover all illnesses because certainly the cost of occasional minor illness is no great hardship even to the individual with a small income, but the cost of a major illness represents a real difficulty. This plan could be offered much more cheaply than one that is all inclusive just as an automobile collision policy with a fifty dollar deductible clause is much cheaper than a complete coverage policy. In a survey made by the Opinion Research Corporation¹⁰ it was found that of the 63 per cent of people who thought that something could be done about making it easier to pay for illness, only 5 per cent wanted it to apply to the ordinary doctor bills. Although there are many plans operating in a number of states in the United States and in several foreign countries, there is no national plan providing medical care in the United States. The state plans apparently have been very suc-

cessful It is difficult to understand why such an obvious need should not be sponsored on a nationwide basis There are many prepayment plans for medical care in operation throughout the United States but at the present time, according to McCann,¹¹ there are no state programs that sell complete medical care

As long ago as 1934, the American College of Surgeons recognized the need for some program to decrease the financial burden of illnesses in persons with moderate incomes On June 10, of that year, the Board of Regents of the College of Surgeons accepted the report of their Medical Service Board¹² which had studied the problem extensively The following are excerpts from this report "The American College of Surgeons affirms its interest and its desire to cooperate with other agencies looking toward the provision of more adequate medical service to the whole community The College believes that it is its duty to the medical profession to assume leadership in this movement and to take control of all measures directed to this end The College recognizes for immediate study four groups of the population for whom more adequate medical service should be made available as follows (a) the indigents, (b) the uneducated and credulous members of the community, (c) those who because of limited resources are unable, unaided, to meet the cost of serious illness and hospitalization, and (d) those living in remote districts where adequate medical care is not obtainable The American College of Surgeons recognizes the periodic prepayment plan providing for the cost of medical care of illness and injury of individuals and of families of moderate means offers a reasonable expectation of providing them with more effective methods of securing adequate medical service" Unfortunately, these recommendations were not only not accepted by the profession generally, but were actually opposed Had the suggestions made by this body been put into operation on a nationwide basis, I believe that the problem of inadequate medical care would have been solved by this time The National Physicians Committee for the Extension of Medical Service has done and is doing a great deal in emphasizing the need for plans to make payment for illness easier, as evidenced by their statement of policy "Steps must be taken to make available to the indigent and low income groups the most effective medicine, medical practice and hospitalization that can be provided and generally provide the widest possible distribution of the most effective methods and equipment in medicine and surgery"¹⁰ Unquestionably their ideas are sound and their program should be supported because it is the one body which has attempted to formulate a constructive plan

In the interest of the patient, the organization and administration of the plans for periodic prepayment of medical and hospital costs must be under the control of the medical profession The medical profession must act in conjunction with the hospitals and such other allied services as may be involved in the project, together with groups of representative citizens and of industry who are interested in the successful operation of the plan

It would be extremely undesirable for the program to be controlled by the government, because the character of the medicine practiced would be definitely inferior, much more expensive, and less efficient

The principle of free choice of physician and hospital by the patient must be assured to the end that the responsibility of the individual physician to the individual patient will always be maintained. The plans which have been introduced throughout the United States have been almost entirely voluntary, and it is the consensus that voluntary prepayment as practiced by the Blue Cross Hospital Program is preferable. Rhode Island is the only state in which there is compulsory insurance¹³. However, this has been in operation only a year, having completed its first year on April 1, 1944, and the program is for cash disability benefits and does not include medical service or payment for such service.

In this cursory outline of the problems facing our profession today, I sincerely hope that I have been able to convince you of the necessity for providing more places for specialty training in the immediate post-war period and even more important, the exigency of formulating and putting into operation a nationwide prepayment plan for medical care. We must no longer maintain the ostrich-like attitude that there is no need for a change in medical practice and not only not oppose constructive programs but actually formulate and promote a plan which, by permitting periodic prepayment, will remove the curse from illness for the masses of people whose income at the present time does not allow adequate medical care. The promulgation of a constructive plan by the profession on a nationwide basis will reasonably assure the defeat of those measures which provide for federal medicine with its bureaucracies, inefficiencies, and inadequacies.

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TREATMENT OF CARCINOMA OF THE COLON*

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OPERATIVE TREATMENT of lesions of the colon has presented the surgeon with many difficult problems in technic since it concerns an organ whose continuation of function is necessary to nutrition and life, an organ filled with pathogenic bacteria, and one in which anatomic peculiarities make for operative difficulties. Many operations have been devised and popularized to meet and overcome these difficulties. The historical aspect of the bold and ingenious methods of treatment have been presented so well by many writers on the subject that we will only acknowledge our debt to them and refrain from further mention. There is not as yet, and probably never can be, a standardized method of caring for such lesions since they vary greatly in size and metastatic spread, and develop in patients who also may have a myriad of complications and associated diseases. Many surgeons have reported the results of their treatment of lesions in this organ, but the total number of patients treated under varying conditions of disease and type of operation is still too small to be statistically convincing. Progress will come with the summation of the experience of all working in this field. In order to contribute to the final total we are reporting here observations on the treatment of 173 patients with carcinoma of the colon proximal to the rectosigmoid junction, managed in the University Hospital between January 1, 1940, and September 1, 1944. Our purpose in reviewing this series was to evaluate our results in the treatment of carcinoma of the colon at the time when we were attempting to utilize primary end-to-end anastomosis, insofar as this method seemed safe and feasible. This communication will not concern itself with end-results, but will be confined to a discussion of the immediate results of operative treatment of the patients entering the University Hospital primarily for relief of their diseases. The end-results will be presented later.

These patients include all cases treated by the permanent and resident staff. The operations were performed by fourteen different surgeons, most of them, however, were performed by the senior surgeons.

TABLE I
SITE OF CARCINOMA OF COLON EXCLUSIVE OF LESIONS OF RECTOSIGMOID
TREATED FROM JANUARY 1940 TO SEPTEMBER 1944

Right colon cecum ascending colon and hepatic flexure	60
Transverse colon	21
Splenic flexure	9
Descending colon	13
Sigmoid colon	70
Total cases	173

* Read before the Fifty-sixth Annual Session, Southern Surgical Association, December 5-7, 1944, Hot Springs, Va

In Table I, is shown the site of origin of the cancer in relation to the part of the colon involved by the primary lesion. These figures only confirm the observations of many others and present no subject for comment.

TABLE II

TREATMENT OF CARCINOMA OF THE RIGHT COLON AND HEPATIC FLEXURE

1 Palliative (nonresectable lesions)	Number	Deaths	Mortality
Ileotransverse colostomies		3	23.0%
Open anastomosis	4		
Closed anastomosis	9		
Total	13	3	23.0%
2 Resectable lesions			
One stage right colectomies	6	0	0
Two stage right colectomies			
(1) Ileotransverse colostomy			
Open anastomosis	22		
Closed anastomosis	18		
(2) Right colectomy	40	1	2.5%
Obstructive resection	1	0	0
Total resectable lesions right colon	47	1	2.15%
Total	60	4	6.6%

In Table II, is shown an analysis of patients presenting themselves with carcinomas of the right colon. They are divided into two groups: first, those in which the lesion was not resectable or in whom resection was not worth while because of extensive metastases, and, second, those in whom the lesion was resectable. In the latter group the primary lesion was resectable but it also includes many patients with metastases or distant spread in whom resection was clearly only a palliative measure. Resection was always effected if it was thought that cure might result and also when it was felt that it would add to the comfort and longevity of the patient even though cure would not be possible because of the presence of metastases. Since studies on lymphatic spread of carcinoma (Coller, Kay and MacIntyre¹) show that lesions in the cecum, ascending colon, hepatic flexure and in the right transverse colon may spread in a retrograde fashion to involve lymph nodes in the ileocecal angle, we carry out excision of the right colon including the lower ileum to the midtransverse colon in lesions lying between these points. This insures a removal of the maximal area of nodal involvement.

Sixty patients with cancers of the right colon were treated. In 13 of them palliative side-tracking operations, ileotransverse colostomies were carried out. Resection of the primary lesion was impossible or was unwise because of massive metastases to the liver in eight patients and widespread peritoneal involvement in five. Combinations of these spreads were present. Three of these patients died while in the hospital, two were deeply jaundiced, with extensive liver metastases, one died on the seventh postoperative day and the other 21 days following the operation. A third patient with extensive liver and peritoneal metastases died of pneumonia seven days following opera-

tion There was no evidence of peritonitis in any of them but we can only assume that there was no disruption of the anastomosis since autopsy was not obtained Ten others left the hospital in an average of 17 days following side-tracking of the primary lesion All patients in this group were beyond the hopes of cure by any surgical attack

In 47 patients the lesion was resected In six patients it was carried out in one stage with closed method of anastomosis, without event In 40 patients the lesion was resected by the two-stage procedure which we have felt is the safest one since the study of our results in such cases by Ransom in 1939² In 22 patients the preliminary end-to-side ileotransverse colostomy was performed by the open method and in 18 by the "aseptic" method None of these patients died following this preliminary operation Right colectomy was carried out as a secondary operation following the preliminary anastomosis One patient died following a second-stage right colectomy of a duodenal fistula on the 43rd postoperative day The primary lesion was an extensive one involving the adjacent retroperitoneal structures and duodenum Post-mortem examination showed a duodenal fistula with carcinomatous involvement of the retroperitoneal structures, the liver, peritoneum and duodenum, a lesion hopeless for surgical excision One obstructive resection was carried out for a lesion in the hepatic flexure The mortality for resection in this series is 21.5 per cent, in contrast to our mortality in 1939 as reported by Ransom as 20 per cent As noted, the single operative death following right colectomy was in the instance of an incurable lesion There were no deaths in patients in whom cure might be hoped for The total hospital mortality for all patients with carcinoma of the right colon both hopeless and resectable was 6.6 per cent

There are several different methods of surgical approach to the problem of right colectomy for carcinoma Lahey, *et al*³ advise exteriorization of the colon and ileum following resection with subsequent closure of the stomas Whipple⁴ urges the importance of the routine use of the Miller-Abbott tube near the site of the anastomosis following a one-step resection Mayo⁵ advocates the one-stage resection All of these methods have importantly reduced the mortality in the hands of their advocates We realize the importance of flexibility and individualization of surgical procedure but further personal experience has served only to satisfy us with the two-stage operation in most cases of cancer of the right colon, as described by Ransom in a study of carcinoma of the right colon Small lesions may be resected in one stage by the experienced operator, with brilliant results If the lesion is fixed, infected or extensive, requiring wide dissection with removal of the mesocolon and the abdominal wall, this emphasizes the value of the two-stage operation There are two phases to the treatment, one, restoration of the continuity of the gastro-intestinal tract, and two, an extensive intraperitoneal dissection with associated widespread traumatic peritonitis If anastomosis of small to large bowel is made at the same time as the extensive resection, the fate of the function of the anastomosis is dependent upon the anastomosis plus the asso-

ciated traumatic peritonitis. Intra-ileal decompression certainly is necessary and indicated under these circumstances. We feel that with a preliminary anastomosis carried out under a controlled technic, either the open or closed method, with quick restoration of the function of the bowel through the new channel, ileus and its concomitant symptoms are reduced to a minimum. We have rarely been obliged to decompress the small intestine following ileo-transverse colostomy. When this anastomosis functions, the right colectomy can be carried out with its associated traumatic peritonitis without marked interference with the function of the gastro-intestinal tract. Stage operations have drawbacks, since each stage carries the dangers of any operation, but our experience causes us to continue to adhere to this procedure in this instance for the reasons given. The use of the transverse incision and early mobilization of patients has cut down the hospitalization time with this two-stage procedure until the time element is no longer an argument against it. We have been impressed with the importance of the transverse incision and this approach is now routine in our clinic, in both right and left colectomy. It will be discussed later in this paper.

TABLE III
TREATMENT OF CARCINOMA OF THE TRANSVERSE COLON

1 Palliative	Number	Deaths	Mortality
Celiotomy and peritoneal drainage	1	1	100%
Cecostomy with peritoneal drainage	1	1	100%
Total	2	2	100%
2 Resectable lesions			
Primary end to end anastomosis	11		
Open anastomosis	2		
Closed anastomosis	9	1	11%
Obstructive resections with partial resection			
stomach and jejunum	4	2	50%
Complementary cecostomies	8		
Preliminary cecostomy	1		
Two stage right colectomies	4	0	0%
Open anastomosis	3		
Closed anastomosis	1	0	0%
	19	3	15.8%
Total	21	5	23.8%

Carcinoma of the transverse colon frequently involves adjacent organs especially the stomach and jejunum and offers more difficult problems for surgical eradication. Table III, sums up the results in the treatment of 21 such lesions. Some lesions involving the right transverse colon were grouped with the lesions of the right colon as previously discussed. Two patients with an obstructing lesion of the transverse colon were admitted with perforation of the cecum and widespread peritonitis. They were treated by celiotomy with drainage and cecostomy, with death in both cases. Of the resectable lesions, ten were treated by excision and end-to-end anastomosis by open or

CARCINOMA OF THE COLON

closed methods There was one death in this group following resection of the primary lesion, with a partial gastrectomy and resection of the involved jejunum This patient died from shock on the second postoperative day In four other patients extensive resections of the colon, stomach and jejunum were carried out for widespread carcinomatous involvement, with exteriorization of the ends of the colon Two of these patients died, one on the tenth postoperative day of peritonitis, and a second on the first postoperative day of myocardial infarction In four patients with a lesion in the midtransverse colon, two-stage operations were carried out in the right colon without mortality The mortality following resection of lesions of the transverse colon was 15.8 per cent, and the total mortality, including two patients with general peritonitis from perforation, was 23.8 per cent The deaths from resection were all in patients with wide spread lesions involving adjacent organs in whom extensive resections of stomach and jejunum were carried out and in whom the hope of cure was slight

TABLE IV
TREATMENT OF CARCINOMA OF THE SPLENIC FLEXURE

End-to end anastomosis	Number	Deaths	Mortality
Closed	4	0	0%
Open	1	0	0%
Cecostomy			
Preliminary	1		
Complementary	4		
Obstructive resections	4	1	25%
Total	9	1	11.11%

The splenic flexure offers great operative difficulties because of the intimate relation of the lesion with the stomach and spleen As shown in Table IV, there were nine patients with lesions at this site Five of them were treated by resection with end-to-end anastomosis, without mortality

Four patients were treated by resection of the obstructive type, one of whom died This patient had a large lesion involving the jejunum, with perforation and abscess formation The splenic flexure and a portion of the jejunum were resected and the abscess cavity drained, a hopeless case in which gross carcinoma was present on the peritoneum and in the deep mesenteric nodes beyond the reach of removal, he died of operative shock on the first postoperative day The mortality following resection of carcinoma in this segment of colon was 11.11 per cent The one death was a patient with a hopelessly far advanced carcinoma

In Table V, is shown the results of treatment of 13 patients with lesions of the descending colon, nine were treated by resection with primary anastomosis and four by resection of the obstructive type There were no hospital deaths In most of these patients the splenic flexure was removed and an anastomosis was made between the transverse and the lower portion of the descending colon or with the upper end of the sigmoid colon

TABLE V

TREATMENT OF CARCINOMA OF THE DESCENDING COLON

End to-end anastomosis	Number	Deaths	Mortality
Closed	6	0	0%
Open	3	0	0%
Preliminary cecostomy or colostomy	4		
Complementary cecostomy	5		
	—		
Obstructive resections	4	0	0%
	—	—	—
Total	13	0	0%

TABLE VI

TREATMENT OF CARCINOMA OF THE SIGMOID COLON

1 Palliative (nonresectable lesions)	Number	Deaths	Mortality
Celiotomy—only	1	0	0
Celiotomy with colostomy	11	1	9.9%
Cecostomy—peritonitis	1	1	100%
	—	—	—
Total	13	2	15.4%
2 Resectable lesions			
End to end anastomosis	51		
Closed	30	0	0
Open	21	1	4.7%
Obstructive resections	6	0	0
	—	—	—
	57	1	1.8%
	—	—	—
Total	70	3	4.2%
Preliminary cecostomy	12		
Preliminary colostomy	8		
Complementary cecostomy	31		
No decompression	6		

In Table VI, is shown an analysis of the patients presenting lesions of the sigmoid colon exclusive of lesions involving the rectum or the recto-sigmoid junction. There were 70 patients of whom 13 were nonresectable. In one of the 13 patients cecostomy was performed for symptomatic relief of obstruction, however, he succumbed to peritonitis already present as a result of perforation. Celiotomy alone was carried out in one patient with a frozen pelvis and extensive peritoneal and hepatic metastases. In the remaining 11 cases, celiotomy with colostomy was performed. Resection was impossible or deemed not worth while in seven of the 11 patients because of extensive hepatic metastases, and widespread peritoneal involvement, and in four patients, because of a fixed lesion in the pelvis in addition to extensive peritoneal metastases. Pulmonary embolism was the cause of one death following colostomy. In the treatment of these hopeless lesions, the mortality rate was 15.4 per cent.

In 57 patients of this group, the lesions were resected by the aseptic method in 30, by the open method in 21 and by obstructive methods in six. In 32 patients there was no gross evidence of any spread of the disease and cure can be hoped for. In 21 patients there was gross evidence of the presence of unremovable cancer and the resection could only be palliative in effect. Of these, 13 had hepatic metastases, six presented peritoneal spread and 11

two the lesion involved the bladder. The involved area of the bladder was resected but recurrence was considered probable. Multiple lesions of the bowel were encountered in six patients in whom segments of the ileum were resected and restoration effected by end-to-end anastomoses. In two patients two separate carcinomas of the colon were encountered, both being resected and continuity restored by the aseptic end-to-end method. It is of interest to note that in six patients with extensive local and peritoneal involvement, resection of the obstructing lesion was carried out and the anastomosis was made between bowel ends, the peritoneal surfaces of which were invaded by carcinoma, all united without event. In the 57 patients upon whom resection of a primary lesion was performed there was one death, a mortality of 1.8 per cent. This patient died of peritonitis due to the employment of an unwise technical method. A rubber tube was placed in the descending colon some inches above the site of anastomosis for purposes of decompression. The tube was pulled out by the patient with resultant fecal spread and peritonitis. A cecostomy would have been preferable and probably would have obviated the complication.

TABLE VII
SUMMARY OF THE MANAGEMENT OF CARCINOMA OF THE COLON AND MORTALITY

	Number	Per Cent
Lesions resected	145	83.8
Lesions not resectable		
Palliative operation	28	16.2
<hr/>		
Of lesions resected		
(a) Other gross carcinoma—irremovable		
(1) Liver metastases	20	
(2) Peritoneal carcinomatosis	13	
	<hr/>	
	33	19.1
(b) Gross carcinoma removed—with cure possible	112	64.7
	<hr/>	
Resection mortality		4.1
Over-all mortality		7.5

In Table VII is presented a summary of the management of the carcinomas of the colon. Twenty-eight patients, or 16.2 per cent, presented lesions in which resection was impossible or deemed not worth while because of the extensive spread of the lesion. In 145, or 83.8 per cent, the primary lesion was resected. In 33 patients, or 19.1 per cent of those resected, there was present gross carcinoma other than the primary lesion which was beyond the reach of surgical excision. Among these, 20 patients had hepatic metastases and in 13, there was extensive peritoneal spread. Thus, resection in this group can be only palliative in effect. In 112 patients, or 64.7 per cent, resection was carried out in patients in whom there was hope for cure. Lymph node involvement was of course present in many of this group. Exact studies of the extent of nodal metastases were not carried out and because gross methods of determining their presence are inaccurate their incidence is not definitely known. Previous studies by Collier, Kay and MacIntyre¹ showed involve-

ment of 62.5 per cent of nodes in resected carcinomas of the right colon and 60 per cent in nodes in resected carcinomas of the left colon. These findings are probably essentially applicable to the lesions here presented. The over-all hospital mortality for the entire group of 173 patients presenting themselves for treatment is 7.5 per cent. The mortality in patients in whom resection was carried out was 4.1 per cent. To summarize the causes of death, four occurred in patients having extensive resection of transverse colon or splenic flexure with stomach and jejunum in an attempt to remove widespread carcinoma, one occurred from a duodenal fistula following right colectomy, autopsy proving the presence of unremovable cancer. Had these patients survived, their hope for cure would have been exceedingly small. One patient died of sequelae following injudicious selection of operative method. Thus, among the patients in whom cure might be effected there was in reality only one death due to faulty technic presenting a mortality rate of 0.89 per cent.

These observations emphasize the fact that the surgical treatment of carcinoma of the colon susceptible to surgical eradication is much better than is our ability to get patients for treatment at a time when the lesion is removable. The outstanding need for better results is earlier diagnosis. The mortality of surgical treatment in patients with cancer of the colon when the lesion is localized is low. Surgical treatment of lesions that have spread from the primary source carries a higher mortality and small hope of cure.

COMMENT—For many years we employed exteriorization operations in our clinic, first the Mikulicz procedure, then the Rankin obstructive resection with far better results. These procedures minimized the danger of peritonitis but they were marred by a multiplicity of operations, a long hospital stay, fecal drainage, infected wounds, and weak scars. Because of our dissatisfaction with these factors, we decided to attempt a more extensive use of primary anastomosis. In the treatment of carcinomas of the colon in this series, we have endeavored to perform resection with primary anastomosis whenever feasible. The question whether to perform a closed or open anastomosis confronts the surgeon. In this series we have used the open methods in 52 patients and the closed or aseptic method in 68 patients. The aseptic method has become increasingly more popular with our surgeons. It is felt that both methods are satisfactory, peritonitis is unlikely to occur from any local contamination of the peritoneum attendant upon the open anastomosis. Generalized peritonitis occurs from persistent leak of an anastomosis, severe wound infection or as a result of contamination by rare virulent organisms. The striking point of difference between the two methods is not that peritonitis is more apt to occur with one method or the other, but that with any open anastomosis there is a high risk of contamination of the abdominal wall with an increased risk of infection at that place. The peritoneum will withstand infection much better than will the abdominal wall.

In 1939, Collier and Valk⁶ presented before this Association the use of

delayed closure of abdominal wounds that were contaminated by the contents of the gastro-intestinal tract Pemberton and Black,⁷ and A W Allen⁸ since, have reported favorably upon the use of this method In Figure 1, is illustrated the delayed closure of the transverse abdominal wound

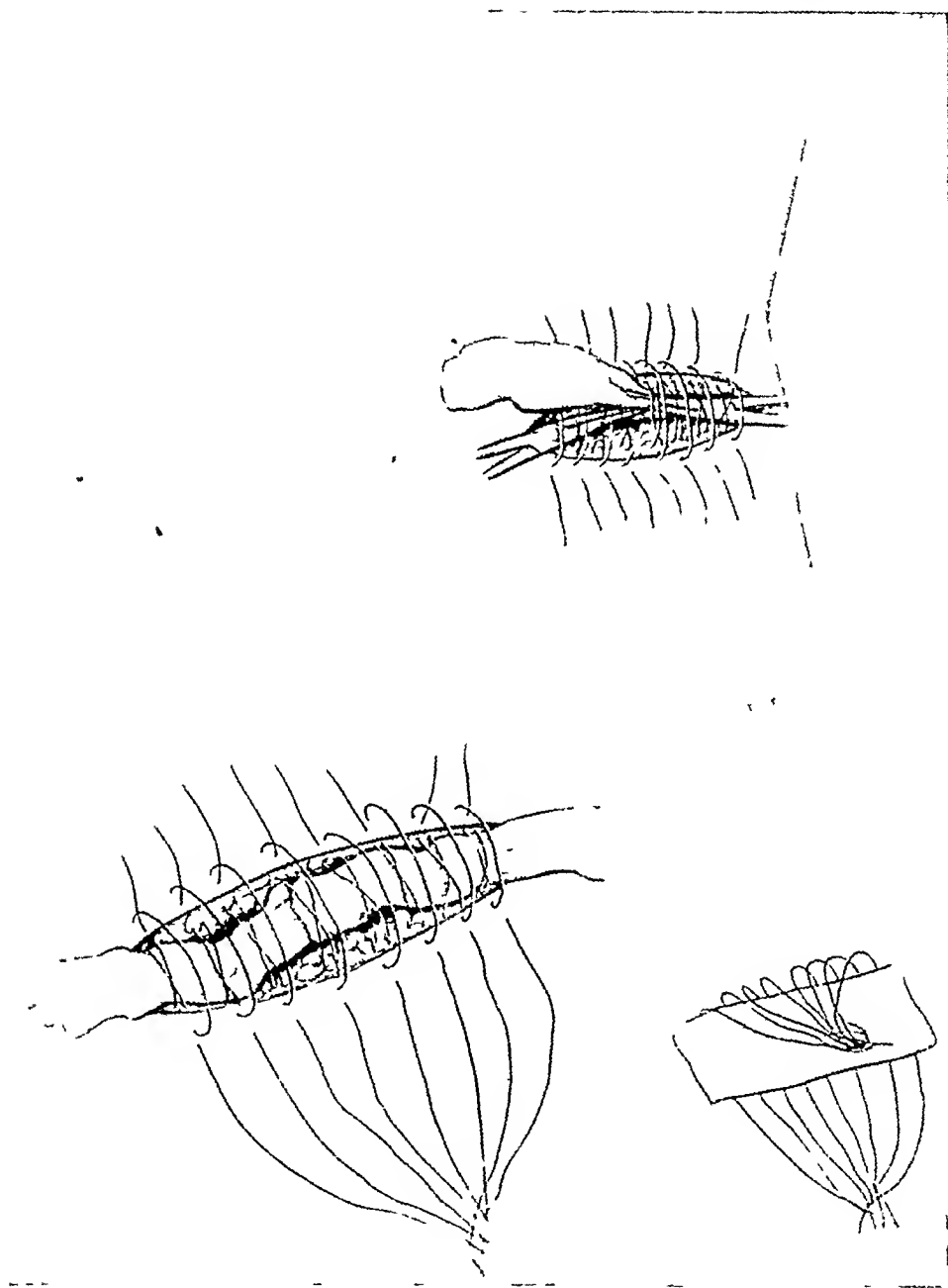


FIG 1—Delayed closure of skin and panniculus of a transverse abdominal incision
Showing gauze in place, which is removed and sutures tied in 48 hours

The peritoneum and fascia are closed in separate layers Gauze is placed in contact with the subcutaneous tissues It is removed in 48 hours and the wound approximated by tying the sutures We have continued to use delayed closure of the abdominal wound whenever open anastomosis has been used, whenever there has been gross soiling from the gastro-intestinal tract, and in closure of colostomes or other fistulous openings in the gastro-

intestinal tract with satisfactory results. In Table VIII, the results of delayed closure of contaminated wounds occurring in this series are shown. There was a resultant infection in 8.4 per cent but these were all minimal and did not lead to dehiscence of the wound or prolonged healing. The method has justified itself in our hands. The chief point in favor of an aseptic form of anastomosis is that the wound may be closed primarily,

TABLE VIII

INCIDENCE OF WOUND INFECTION USING THE DELAYED TYPE OF CLOSURE
WHICH WAS USED ONLY IN GROSSLY CONTAMINATED WOUNDS

1 Delayed Closure—71		
(a) With infection	6	
(b) Without infection	65	
Per cent of infection		8.4

if the open method is used, one should assume that the wound in the abdominal wall is contaminated and delayed closure should be employed. In performing the closed type of anastomosis we have used clamps with a narrow blade, employing an outer layer of silk mattress sutures and an inner suture of fine catgut inserted by the Cushing right-angle method. Clamps are applied at a right angle, unless there is a discrepancy in the size of the lumen of the two segments. The bowel wall must have an adequate blood supply and be approximately normal in its histologic state. If primary suture is carried out, tension must never be present, the bowel is never dissected from its appendages or mesentery in order to secure cleared serosa for approximation. The peritoneum covering the mesentery and the appendages will unite when approximated if the blood supply is undisturbed. The anastomosis is supported by peritoneal flaps and the omentum whenever possible.

In the closure of colostomies we have abandoned the use of crushing clamps applied to spurs. The colostomy is freed from the abdominal wall, an appropriate end-to-end anastomosis is made and the abdominal wall is closed by the delayed method. We have had no misadventures from the use of this method. It appears to us safer, simpler and time-saving as compared to other methods. Obstructive resection still has an important place in the treatment of carcinoma of the colon when the bowel, due to infection, obstruction or associated lesions, is not suitable for primary anastomosis, but to employ it routinely for fear of contamination of the peritoneum at the time of resection is not justified by this experience.

Stenosis of the bowel may occur following the contraction of the scar of a primary anastomosis. In three patients in this series this did eventuate a year or more after operation as shown by roentgenologic studies. In one instance a secondary resection was carried out with restoration of continuity by primary anastomosis, no carcinoma was found and the narrowing of the lumen was undoubtedly due to scar. In two other cases the narrowing in the transverse colon has remained unchanged and without symptoms for two years.

Preoperative decompression is employed whenever obstruction is present. This is common in patients with lesions of the transverse or left colon. Of the patients with resectable lesions of the entire colon, 26 had preliminary decompression. Of these, nine had colostomies and 17 had cecostomies. If rapid relief from distention is desired, cecostomy is performed, if it

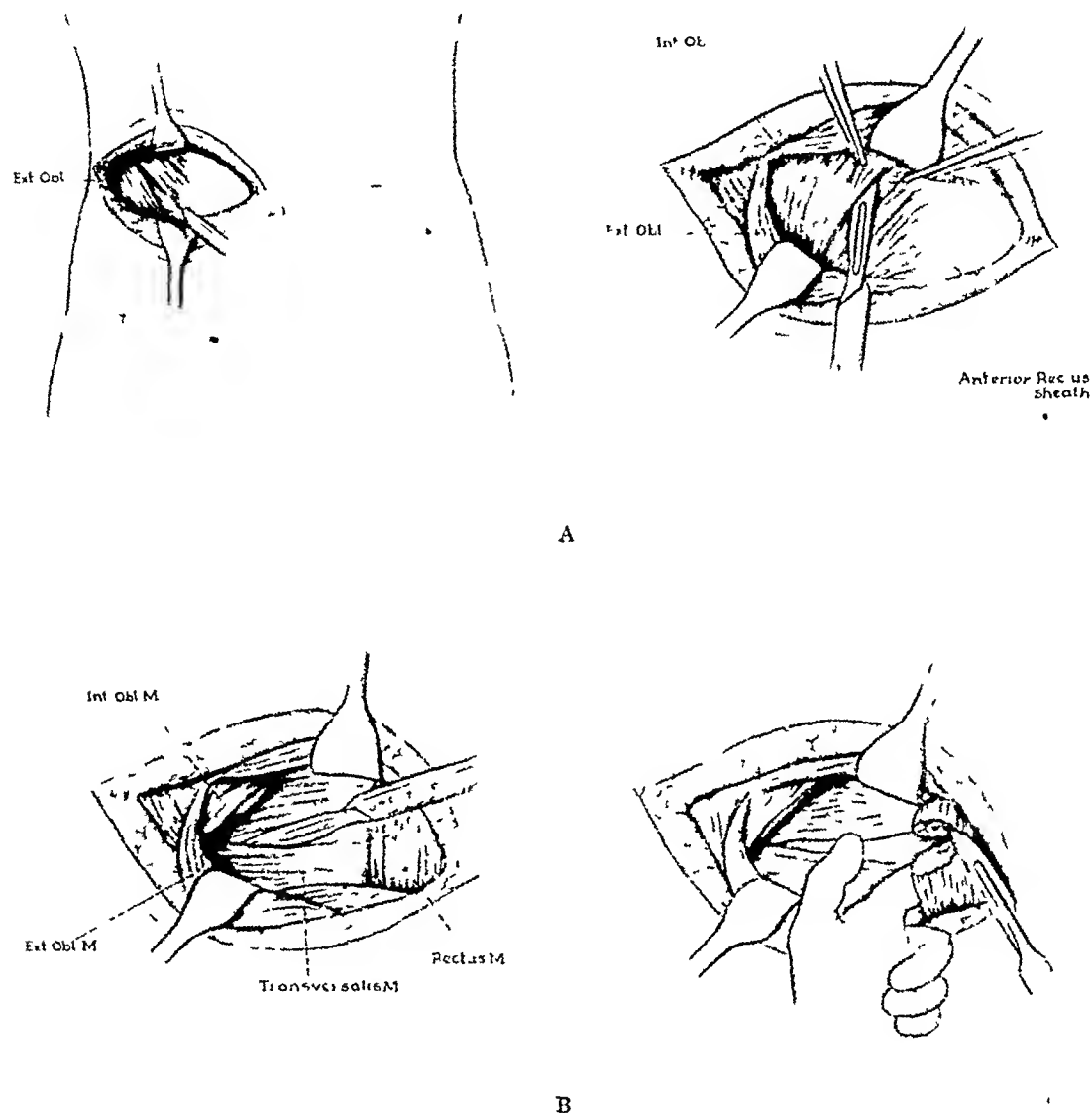


FIG 2—(A) Incision used for right colectomy. External and internal oblique muscles split in direction of its fibers. Left healed transverse scar used for ileotransverse colostomy. (B) Transversalis muscle split in direction of its fibers and rectus muscle cross cut in part or in whole depending upon exposure needed.

is thought that the colon is filled with solid contents and evacuation will be difficult and if the colon is not greatly distended a colostomy is carried out. We do not routinely defunctionalize the left colon by transverse colostomy before performing end-to-end anastomosis in that organ. In those cases in which obstruction was not present and upon whom resection with end-to-end anastomosis was carried out, a complementary cecostomy was performed in all but six patients and a cecostomy was performed following

operation on one of these because of distension. Cecostomy or colostomy before operation is necessary in obstructing lesions, complementary cecostomy adds to the comfort of the patient and is a worthwhile safeguard. The type of cecostomy performed is a slight modification of the Hendon enterostomy or an appendicostomy. Large tubes are not employed. The incision in the abdominal wall is of the muscle-splitting type placed laterally just above and slightly medial to the right anterior superior spine. The great majority of these closed spontaneously within a short time following removal of the catheter. It is a minor safeguard.

We have employed with increasing frequency, transverse incisions in the abdominal wall for operations on the colon until it has now become a routine. The level of the incision is varied to meet the site and situation of the lesion. In Figure 2 is illustrated the method used. The rectus sheath is cut across and a part or all of the rectus muscle is cut perpendicular to its fibers and the flat abdominal muscles are split in the direction of their fibers. This incision gives ready access to the right or left gutter and the colon. This incision lends itself well to obstructive resection as the bowel ends can be brought through the outer angle of the wound without tumor, giving excellent exposure for primary anastomosis. Dehiscence of this type of wound has not occurred. Should infection supervene, the wound does not tend to separate, small intestine does not become adherent to such a wound as it may in those made longitudinally. The wound is more comfortable. We have practiced early rising following operation in patients in which obstruction or infection is absent, routinely, having them get out of bed on the day following operation. It is our belief that this maneuver shortens convalescence and adds to the comfort of the patient. Without endeavoring to present here statistically the advantages, one can say that the abolition of the catheter and bedpan from the post-operative period makes it popular with the patients and alone justifies the method.

The sulfa drugs were used locally and generally in a few patients treated in the early cases of the series. They have not been used locally in any cases operated upon since July, 1940, and they have been used generally only in those patients with peritoneal, urinary or pulmonary infection.

Sulfaguanidine and sulfasuxidine were used as a preoperative measure in a few cases but they have not been used as a routine. From previous experience we feel that the local peritoneal use of the sulfa drugs is unnecessary. The deliberate failure to use any of these chemicals is not an indictment against them but it is felt that the eventual valuation of their utility will be aided by providing a series of patients treated without their use as a series of controls. In no case was vaccination of the peritoneum by any method carried out.

In Table IX, is shown the average number of postoperative days of hospitalization following the different types of treatment. The number of patients in each group is not large enough to make these figures more

than roughly indicative of the facts. Hospitalization of patients with closed anastomosis was shorter than of those with the open type of anastomosis. This was due to a greater incidence of wound infection following the open anastomosis. Even with the delayed method of closure there occurred 8.5 per cent of wound infection that prolonged the hospitalization. The average hospitalization time for patients with open anastomosis was lengthened by a prolonged hospital stay of three patients with severe wound infection in

TABLE IX
SHOWING AVERAGE POSTOPERATIVE HOSPITAL STAY WITH VARIOUS TYPES OF
SURGICAL PROCEDURES FOR CARCINOMA OF THE COLON

End-to-end anastomosis—closed	16.3 days
End-to-end anastomosis—open	26.7 days
Obstructive resections	60.9 days
One-stage right colectomies	14.0 days
Two-stage right colectomies	18.0 days
Palliative (nonresectable) lesions	20.5 days

which delayed closure was not employed. The contrast between hospitalization time of patients with obstructive resections and those with direct anastomosis is striking. In determining hospital stay for patients with obstructive resection, we have included the time of the second entry for closure of the colostomy. The difference in hospital stay between the one- and two-stage right colectomy is not striking and the slightly longer hospital stay of patients with the two-stage operation is not an important criticism of it. The length of hospitalization before operation was not tabulated as it varies so much with conditions of disease and its complications. The utmost importance of careful and thorough preparation of patients for operation has been so well and frequently discussed that the details need not be further emphasized. Suffice it to say that decompression of the bowel must be complete, the patient's nutritional deficiencies overcome, insofar as is possible and anemia corrected by transfusion, thus making the preoperative time element entirely dependent upon preparation.

SUMMARY

A series of 173 patients with carcinoma of the colon treated by operation is reported.

Of these lesions 16.2 per cent presented lesions beyond the reach of resection and for whom only palliative operations could be carried out. Resection of the primary lesion was undertaken on 83.8 per cent of the patients. Of the patients upon whom resection was carried out 19 per cent had other gross metastases in the liver or peritoneum that were beyond surgical removal. Therefore, the resections in this group were palliative in nature.

In 112 patients, or 64.7 per cent, resection was undertaken without evidence of gross carcinomatous spread beyond the lymph nodes, in these cure might be hoped for. Death occurred in only one patient in the group in which there was a chance of operative cure. Deaths occurred from advanced disease or following operative attempts to remove widespread

disease Surgical treatment of carcinoma of the colon will be further advanced by earlier diagnosis of the disease Surgical methods must be individualized to meet the varying conditions of disease

Primary resection with end-to-end anastomosis is feasible in many patients and offers many advantages A complementary cecostomy is a wise safeguard if a proximal vent has not been previously established Open or closed types of anastomosis are equally suitable without fear of peritonitis unless the anastomosis breaks down The abdominal wall is often contaminated during the operation of open anastomosis and wound infection is greater than with aseptic methods of union When the abdominal wall is contaminated, delayed closure of it minimizes the chance and degree of infection The value of the transverse incision is mentioned None of the sulfa drugs were employed routinely and this series may be used as a control in future evaluation of methods of treatment

Improvement in the results of surgical treatment of carcinoma of the colon will come largely from earlier recognition of the disease

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DISCUSSION—DR ALBERT O SINCLETON, Galveston, Texas We appreciate the able presentation of this subject by Doctor Collier His success is quite notable Only a few years ago one was considered to be breaking a cardinal rule of intestinal surgery if he resected any part of the left half of the colon in a one-stage operation At the present time resections and end-to-end anastomoses of the bowel are done with apparent great safety, with a lower mortality and a great saving of time for the patient The excellent results which are being secured with this type of procedure are not necessarily due to the new drugs, such as the sulfonamides, as claimed by some, but to the application of new principles during the last decade These principles consist of first, a proper regard for the circulation of the bowel with careful approximation of viable tissues, preferably with a closed type of anastomosis, second, putting the alimentary tract at complete rest for a period of days subsequent to resection by the use of gastric suction which, if properly used, prevents gaseous distention, and, third, proper care of the patient's fluid balance, electrolytes and food requirements, including glucose and proteids administered parenterally

I also agree with Doctor Collier in his stressing the importance of proper regard for the abdominal wall, with reference not only to infection but more particularly to anatomic incisions We have not found it necessary within the last few years to use a proximal enterostomy for decompression but depend entirely upon gastric suction

CARCINOMA OF THE COLON

DR FRANK P STRICKLER, Louisville, Ky It is certainly a good break for the patient and surgeon when a primary anastomosis of the large bowel can be done, but in a fairly large experience with this type of surgery, how often does this situation present itself? No suture line is better than the blood supply to the part I do not believe that colon cases should be permitted out of bed in 48 hours Why ruin a good operation with bad judgment? The colon does not heal that fast

I do not know positively how much good the sulfa drugs do in colon surgery, but, to date, I see no reason for not using them We at least know that properly given they do no harm, so I will continue to use sulfa drugs in my colon surgery The patient deserves every safety factor available

We are deeply indebted to Doctor Lahey for his resection of the right colon This operation has many applications I have used it for extensive gunshot wounds, intussusception, regional ileitis, as well as malignancy I know that some surgeons object to this operation, but in my hands it has been a life-saver in more than one case The operation is performed with no special instruments, it can be done rapidly and with very little shock I find it a very satisfactory and safe operation

DR JOHN DEJ PRIBERTON, Rochester, Minn I enjoyed Doctor Collier's presentation very much but I do feel that sufficient credit is not being paid to chemotherapy In the fall of 1939, at the Mayo Clinic, we began using sulfanamide compounds in colon surgery in a rather casual manner, occasionally placing 5 to 10 Gm in the peritoneal cavity prior to closure of the wound in cases in which peritonitis was feared because of actual or suspected soiling Later, as experience enlarged, we began using them more routinely In 1942, following the work of Poth and Firor, succinylsulfathiazole was employed routinely as a preparatory measure Other than the use of chemotherapy, there has not been any major change in the management of colonic and rectal carcinoma at the Clinic during the past ten years The hospital mortality rate of all patients with carcinoma of the colon and rectum during the period 1934 to 1943, inclusive, was computed on the basis of the number of patients who had been operated upon, that is, whether they had a resection, a palliative procedure or only an exploratory operation As the graph in Figure 1 reveals, the mortality rate before 1934 varied between 15 and 20 per cent A slight drop occurred in 1939, the year in which sulfonamide compounds were first used intermittently, then in 1940 there was a precipitous drop to around 5 per cent, and the rate has since dropped more During this period of decline in the mortality rate, there has been no decline in the rate of resectability but instead, as indicated in the graph in Figure 2, there has been an appreciable increase

The changes that have occurred in surgery of the colon since the introduction of chemotherapy have been as spectacular and revolutionary as the changes wrought by iodine therapy in surgery of exophthalmic goiter The striking analogy has often occurred to me Just as in the pre-iodine era of thyroid surgery the technical perfection of the surgical procedure of partial thyroidectomy was no definite assurance that the patient would endure the operation (for not infrequently a severe hyperthyroid crisis would supervene, resulting in death), so in the prechemotherapy era of colonic surgery the technically errorless resection of a segment of intestine was not definite assurance that the patient would survive, for not infrequently infection would spread and produce fatal peritonitis The surgeon in both fields, after resorting to refinement of technic and other measures, finally learned that the best means of combating the hidden danger (acute hyperthyroidism on the one hand and the spread of infection on the other) was to divide the operation into stages In both fields the employment of the two-stage procedure resulted in great improvement but only partially eliminated the hidden danger peculiar to each Thus, it was only after preoperative iodine therapy had been standardized that the surgeon could be reasonably assured that, barring some accident, the patient with exophthalmic goiter would endure an uncomplicated partial thyroidectomy in one stage And, so, in the field of colon surgery, only in recent years, since the advent of chemotherapy, could the surgeon be reasonably confident that the patient with carcinoma of the colon or rectum would survive an uncomplicated operation for resection of the colon

DR FRANK H LAHEY, BOSTON, MASS Doctor Collier's approach to this problem of carcinoma of the colon is an excellent one because we need to demonstrate again and again what can be done in these cases and what more could be done, if we could

get earlier diagnoses. If we start at the very beginning, the logical approach to this problem of carcinoma of the large bowel is more frequent contrast enemas and more frequent good sigmoidoscopic examinations to discover polypi. We must find polypi more frequently than we do if we really want to approach this problem of cancer of the colon and rectum earlier, because polypi are such real precancerous lesions.

I have repeatedly reported Doctor Swinton's interesting approach to this problem because there is such a lesson in it. Before going in the Army he was particularly interested in the earlier diagnosis of these cases. He took 100 cases of cancer of the right colon in the clinic, proven by removal, 100 cases of cancer of the left colon proven by removal, and 100 cases of cancer of the rectum proven by removal, and asked, not the patient but of the history—"Was there blood in the stool? Was there alteration of bowel function and was there pain of an obstructive character?" The answer was "Yes" in all but 2.3 per cent of the cases. In other words, in 97.7 per cent of the cases the diagnosis, or at least the suspicion of it, was in the history.

I do not wish to consider the technical approach because one can do the same radical operation either by the modified Mikulicz procedure or by primary anastomosis. It is largely a matter of personal opinion. I think you would be much more interested in end-results. Having recently reported on our end-results at a meeting of the Massachusetts Medical Society, I would like to present them to you. We have now operated upon 1800 patients with carcinomas of the colon and rectum, of these, 70 per cent were in the rectum and 30 per cent were in the colon. The total mortality of the entire series, including the early cases, was 10.25 per cent. The mortality in the last 5 years for the entire group was 5 per cent. The mortality in the last two years was 2.7 per cent for carcinoma of the colon and 3.8 per cent for carcinoma of the rectum. The five-year nonrecurrence rate of the entire group of patients who have been submitted to the radical procedure was 50 per cent. If we break this group down into special groups, it illustrates something that we know and have known quite well, that is, it is not the size of the lesion that makes the inoperability, it is particularly the invasion of blood vessels. If we take the group with no lymphatic metastases, no invasion of adjacent organs and no blood vessel invasion, 90 per cent are alive and well over five years, with no recurrence, if we take the group with only lymphatic metastases, 37 per cent are alive and well over five years without recurrence, and if we take the group with involvement of other organs, 30 per cent are alive and well over five years without recurrence. If we take the group with blood vessel invasion, however, only 14 per cent are alive and well over five years after operation.

It will be of interest to demonstrate by follow-up figures whether or not removal of the lesion in the presence of metastases in the liver is worth while. The average length of life of patients with metastases in the liver without the lesion removed is 14 months, while the average length of life of the patient with metastases in the liver and with the lesion removed is 25.5 months. This demonstrates, it seems to me, quite conclusively that, unless the metastases in the liver are extensive, if the lesion is removable it is worth while to resect it even though there be metastases in the liver. In 95 per cent of the patients upon whom we have operated there have been metastases in the liver.

Medicine and surgery can be proud of, but not satisfied with, the results of operations for carcinoma of the colon and rectum. I must again stress the fact that we need particularly to educate the internists and the general practitioners to investigate these patients early for polypi and to stress particularly to the general practitioners and to the public that the presence of the three features which we have described as indications of the presence of possible malignancy of the colon and rectum—alteration in bowel function, blood in the stools and pain of an obstructive character—should cause these patients to be submitted to a complete gastro-intestinal roentgenologic series, contrast enema and sigmoidoscopic examination.

We have just had an interesting experience which demonstrates what has happened in regard to polypi in a group of bank officials sent to us for complete physical examination. Out of the first 25 men in this group sent to us, four had polypi. This is a much higher incidence than we all know regularly exists, but demonstrates that this lesion, which is undoubtedly in many instances a precancerous lesion, is much more prevalent than we think it is, and it is, of course, the stage at which cancer of the rectum and colon should be treated if possible.

CARCINOMA OF THE COLON

DR FREDERICK A COLLIER, Ann Arbor, Mich (closing) I want to thank you for your discussion of this paper, and to emphasize our position in regard to the sulfa drugs We deliberately refrained from using them in this series of cases so there would be a control group, and we invite comparison between this and other similar groups in which the sulfa drugs have been used I am convinced that sulfas in the peritoneal cavity are not worth while and I am, likewise convinced that their use in the abdominal wall is harmful I believe sulfasuvadine has a real place in the preparation of these patients and we are going to use it now that this series is finished

FIG 1

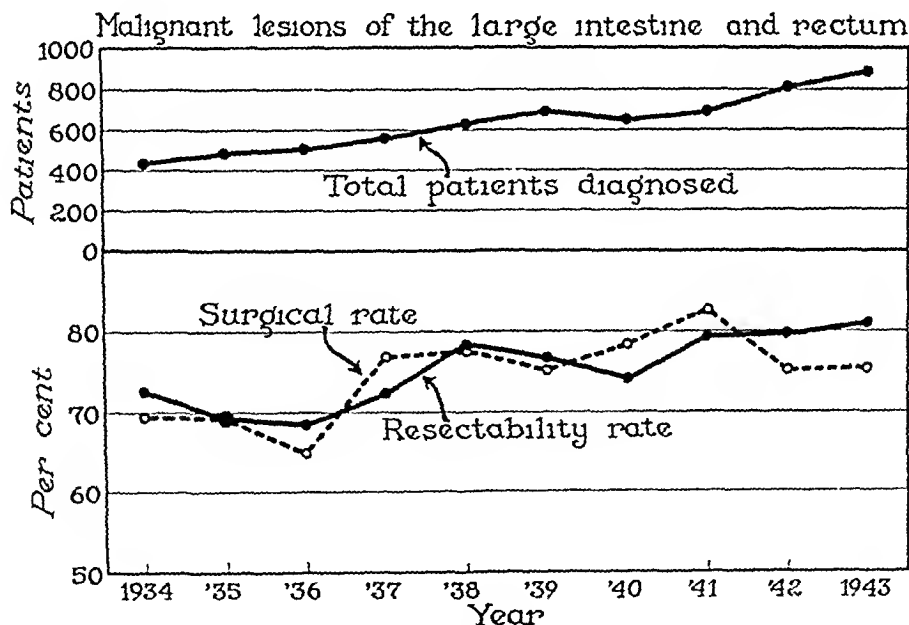
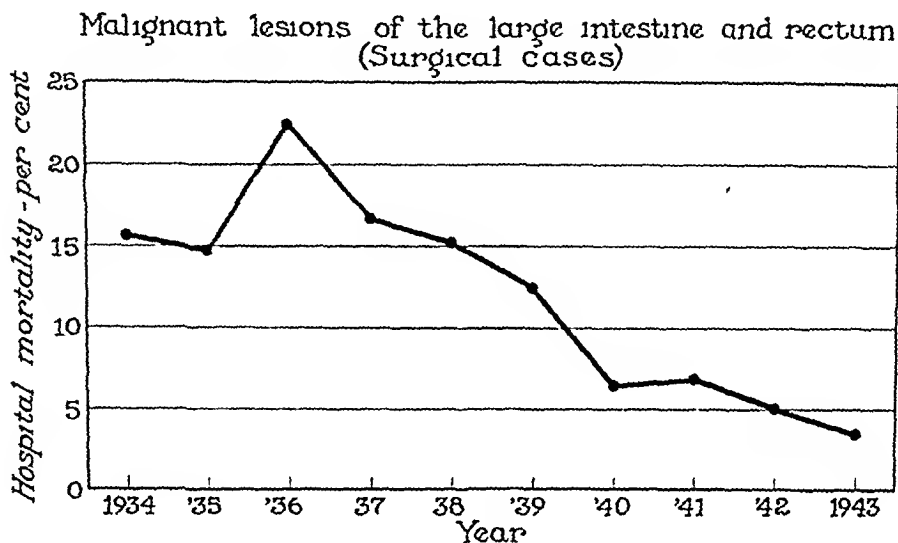


FIG 2

I want to emphasize what Doctor Lahey has said about early diagnosis through knowledge of the history of the disease and frequent examinations with the sigmoidoscope, and routine barium enemas Surgical treatment is far more efficacious than is our ability to make an early diagnosis when the chance for cure is good In this series of cases fatalities occurred from far advanced disease or from heroic surgical treatment carried out in a vain attempt to cure the hopeless lesion The mortality from operative treatment of localized cancer was exceedingly low Primary resection with direct anastomosis is feasible in a high percentage of cases

A METHOD OF RE-ESTABLISHING CONTINUITY BETWEEN THE BILE DUCTS AND THE GASTRO-INTESTINAL TRACT*

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SO MANY OPERATIVE PROCEDURES for the re-establishment of continuity between the biliary passages and the gastro-intestinal tract have been recorded that one hesitates to offer another possible solution to this difficult and complicated problem. I have had so many disappointing sequelae, following the use of what appeared to be the most logical reconstruction for that particular patient under the conditions at the time, that much thought about the whole situation has led to certain deductions.

Many excellent contributions have been made to this subject. The most noteworthy of recent years are represented by the exhaustive report by Ellsworth Eliot, Jr.¹ in 1936, the excellent presentation before this Association by Lahey² in 1936, the work of Pearse³ on the vitallium tube, the method of Wilson⁴ and that of Dragstedt, *et al*⁵. Every surgeon should read Sir James Walton's⁶ superb article in *Surg Gynec and Obst* for July, 1944. The delightful style of this presentation would make interesting reading to any intelligent person whether he be student or master surgeon.

I wish to point out here that I do not plan an exhaustive review of this entire subject and, therefore, hope that many important reports not mentioned will not cause offense. It seems unjustifiable at this time to repeat or even bring entirely up to date the complete complication of Eliot.¹ I desire to discuss the difficulties encountered in some of the procedures I have tried and to present a preliminary report on a method I have found satisfactory in a small group of cases. Some of these had been operated upon by other methods by me, some by others, and most of them several times and by several surgeons.

PREVENTION OF DUCT INJURY

First, and most important of all, is the obvious responsibility of every surgeon to practice and teach the need for the greatest possible respect for the simple "gallbladder." The operation of cholecystectomy is one that is commonly considered within the scope of the surgeon of little experience in this field. These men are often unaware of the high percentage of anomalous arrangements of blood vessels and ducts in this region. Death following cholecystectomy is often thought to be due to causes beyond control and remote from the operative site, yet, doubtless, many are due to unrecognized bile peritonitis or necrosis of the right lobe of the liver. The so-called "liver deaths," once considered due to an unremediable lack of reserve on the part of the patient, were probably often the result of

* Read before the Fifty-sixth Annual Session, Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

ligation of the right hepatic artery under the impression that it was the cystic artery. The frequency of these anomalies was first brought to our attention by Eisendraht⁷ Biowne,⁸ and others, have made further important contributions to this subject. So commonly does one find an arrangement that varies from the so-called normal, that one should constantly be mindful of such possibilities. Fortunately, many of the anomalies are not of such a nature as to interfere with a routine procedure. Some of them, however, are sufficiently important to make a difference between life and death and many will leave a patient in such a condition that I have often wondered whether life as it had become for that particular victim was not worse than death.

This means that every surgeon must obtain adequate exposure of this region. Sufficient dissection of the area must be carried out to identify beyond question every structure that is vital to leave uninjured, and divide only those accompanying the gallbladder itself. Several years ago, I reviewed all the case histories of patients entering the Massachusetts General Hospital with operative injuries of the bile ducts. In every instance, save one, when the type of operation could be ascertained, the surgeon had removed the gallbladder from the ducts towards the fundus. This led me to believe that perhaps it was safer to remove the gallbladder from the fundus toward the ducts. Consequently, I worked out a meticulous technic with artificial edema in the gallbladder peritoneum, which has been used almost exclusively by the resident staff on the East Surgical Service of our clinic for about six years.⁹ During this interval, many anomalies have been recognized and no injuries to the common or hepatic ducts nor to the hepatic arteries have occurred. It is only fair to say that I am not aware of any such catastrophes on the West Service, where they have continued a preference for the dissection from the ducts towards the fundus. Others feel that the operation can be performed just as safely, or even more so, from below upwards. The advantages, particularly of ligating the veins and small accompanying accessory ducts leading from the gallbladder directly into the liver, are certainly worth considering. It is also easier to preserve the peritoneal-like capsule of Glisson in the liver bed if the dissection is from above downward. Often no effort is made to preserve this tissue and it is amazing to see the number of surgeons who apparently have never heard that it could be saved or that such a protective structure actually existed. In fact, a method of routine cholecystectomy has been advocated that leaves the posterior wall of the gallbladder attached, the mucosal surface of which is dissected by electrocoagulation. Frequently, when the dissection is done from the ducts to the fundus, the posterior peritoneal layer becomes accidentally detached from the liver bed, even if only mild upward traction is used on the severed cystic duct. The real disadvantage to the operation from the fundus towards the ducts is that it requires meticulous hemostasis and, therefore, the operating time is increased. Unless the field is dry and clear vision of structures obtained,

the chief indication for this approach is lost. The object is to expose the cystic artery, cystic duct, and at least the common hepatic duct before any important structure has been clamped or divided. It is obvious that the approach is not the important feature but the accuracy with which one identifies the structures to be severed. It seems clear to me that men of less experience should select the type of operation to be undertaken according to the ease of access to the duct region. Then they will not find themselves in a field obscured by bleeding and be faced with uncertainty regarding the structures they have interrupted. In many of the injured duct cases, we obtain the story of a difficult dissection in a bloody field. On the other hand, it is surprising how often the surgeon states that he is sure the common duct could not have been injured because the operation was so easy and went so well.

The second obvious attitude should be early recognition of duct injury. Occasionally, a surgeon will ask for advice by telephone regarding the proper steps to take, having recognized an injury to the common duct, the first in many years of surgical practice. The repair can usually best be made at the time of injury. If not then, as soon as the patient can be safely moved to another hospital. During this interval, liberal external drainage is important. Often the bile flow can be completely controlled by the temporary insertion of suitable tubes. Unless the surgeon has had experience with the repair of ducts, he may wish to give this responsibility to someone else. Too often, a poor repair results in failure and the surgeon suffers as much as the patient. A careful approximation of the ends of the ducts without tension, with nonabsorbable interrupted sutures, will usually give a good result. This can be made easier if done over a suitable tube. It is better to plan on removal of the tube and a separate incision in the duct proximal to the suture line is advised. One may use a T-tube or Horgan's L-tube for this purpose to advantage. One should have in mind the eventual minimum of scar tissue at the site of the anastomosis and avoid, if possible, the additional trauma produced by the removal of the tube if placed in the suture line. Tubes have been left within the duct and not through the papilla of Vater. Such a tube will eventually become incrustated with bile salts whether it is of rubber or vitallium. Long tubes placed well into the jejunum will often spontaneously pass in time but, on one occasion, I had to remove such a tube 14 months after its insertion.

TYPES OF INJURY

The victims of injured bile ducts fall into two main groups. 1. The type that either becomes jaundiced within a few days after operation or drains an unexpected amount of bile into the peritoneal cavity or to the outside. 2. Those patients who do moderately well for some weeks or even months before developing signs of jaundice with beginning episodes of chills and fever.

In the first group, we have patients who have had ligatures placed upon the cut-ends of the ducts with resulting jaundice, usually being

temporarily relieved in a week or ten days by the sudden outpouring of large quantities of bile. Others in this group have an immediate reaction characteristic of bile peritonitis from which at least 25 per cent die¹⁰ or, if drains were adequately placed, the discharge of an abnormally large quantity of bile to the outside. In the group with ligatured ends, the situation may be recognized and corrective surgery instituted before the sutures give way, resulting in a possible fatal bile peritonitis. This accident is most apt to take place where the cystic duct is short or runs into the common duct at a low level. Traction on Hartmann's pouch (ampulla of the gallbladder) brings into view a normal-sized common duct that under tension seems to the operator small enough to be the cystic duct. It is difficult to understand how the surgeon can tie the same duct at a higher level, which he must do in order to get the gallbladder free, without recognizing his error. Probably, he mistakes the upper segment of common duct for the cystic artery. At any rate, I have removed chromic catgut ligatures placed one month before on the proximal and distal ends of the common duct separated by a gap of four centimeters. So much of the duct was missing that mobilization to allow end-to-end suture was impossible. In this case, after an unsatisfactory year of life with reconstruction over a vitallium tube, there has been complete relief obtained by the method I will describe later. Another type of injury, falling into Group 1, is that produced by sufficient tenting of the common duct to allow complete division of this structure. This injury results in a condition lending itself best to an end-to-end anastomosis.

In Group 2, we have the partial strictures that take place when the duct is tented sufficiently to constrict only its anterior portion. Also, in the instance of hurried, blind, hemostatic control of unexpected hemorrhage, the duct may be injured in such a way as to produce a slow stricture with resulting characteristic signs and symptoms. This second type of injury can always be avoided if the surgeon will go to the left side of the patient and place the fingers of his left hand into the foramen of Winslow. By exerting gentle upward pressure, the bleeding is completely controlled until the exact source of the hemorrhage is determined and accurately secured. I have witnessed a brilliant young surgeon spend one hour in the accurate replacement of a slipped cystic artery hemostat when five minutes spent on the opposite side of the table would have sufficed.

If partial duct injury occurs, a gradual onset of symptoms finally brings about complete invalidism. This group of patients will present themselves for help from 6 to 18 months after their first operation. Under these circumstances, one can expect to find that the distal segment of duct is narrowed and often sclerosed to a fibrous cord. On opening the duodenum one finds the papilla of Vater but may not be able to get the finest probe through it. Experiences such as these have led me to feel that in Group 2, one should abandon any hope of finding a sufficiently normal distal segment to warrant attempts at end-to-end anastomosis. In this group, one finds

that the reconstruction procedure, which I am about to describe, of real value. When one abandons the distal segment of the duct and attempts anastomosis between the proximal dilated segment and the gastro-intestinal tract, there are certain principles that must be understood or a high percentage of failures will result.

PRINCIPLES INVOLVED IN RECONSTRUCTION OF BILE DUCTS

That man can not duplicate nature's connection between the biliary system and the gastro-intestinal tract is obvious to all who have attempted

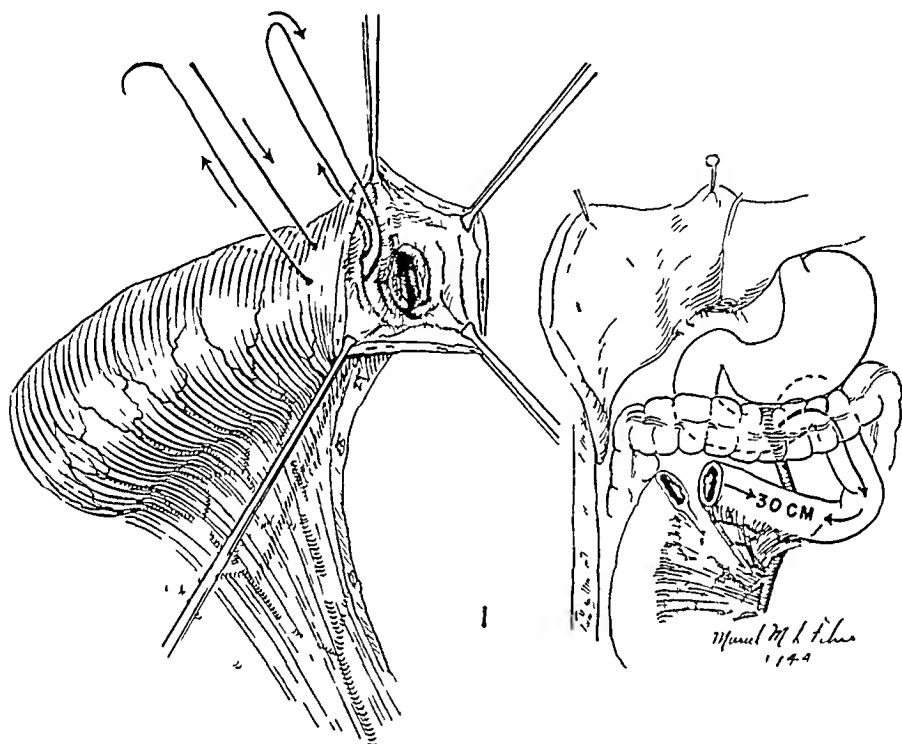


FIG 1.—Schematic drawing representing the division of the jejunum approximately 30 cm. distal to the ligament of Treitz. Also, the method which is used to invert the end of the distal segment.

it. When we think of the ease with which permanent anastomoses are made in the gastro-intestinal tract with effective by-passing of its contents, it seems strange at first that such is not the case between the biliary system and the intestine. One is familiar with the term "sphincter of Oddi" and much has been said about preserving its integrity. Recently, Gordon-Taylor¹¹ has challenged the sphincter mechanism of the outlet of the bile duct and stated that there are only longitudinal and oblique muscle fibers in this region. He believes that any control of contents from the bile ducts into the intestine would have to be explained on the basis of an erector influence of these muscle fibers on the papilla. It is known to us that the duct passes through the duodenal wall in an oblique direction and that we can stretch or cut these muscle fibers with impunity when the occasion demands. It seems that nature has protected us from serious injury in this respect. The oblique direction of the duct through the duodenal wall, which is

RECONSTRUCTION OF BILE DUCTS

further supported by the adjacent pancreas, may leave an overhang of duodenal mucosa to act as a flap valve. This may explain the infrequency of "duodenal reflux" and "ascending cholangitis" when the normal relationship between the ducts and the duodenum are maintained.

Why anastomoses between the gallbladder or ducts to the gastro-intestinal tract so often result in cholangitis is not easy to understand. Certainly, two factors are worthy of consideration. The peristaltic action of the gastro-intestinal tract will send its contents into the liver ducts.

FIG 2

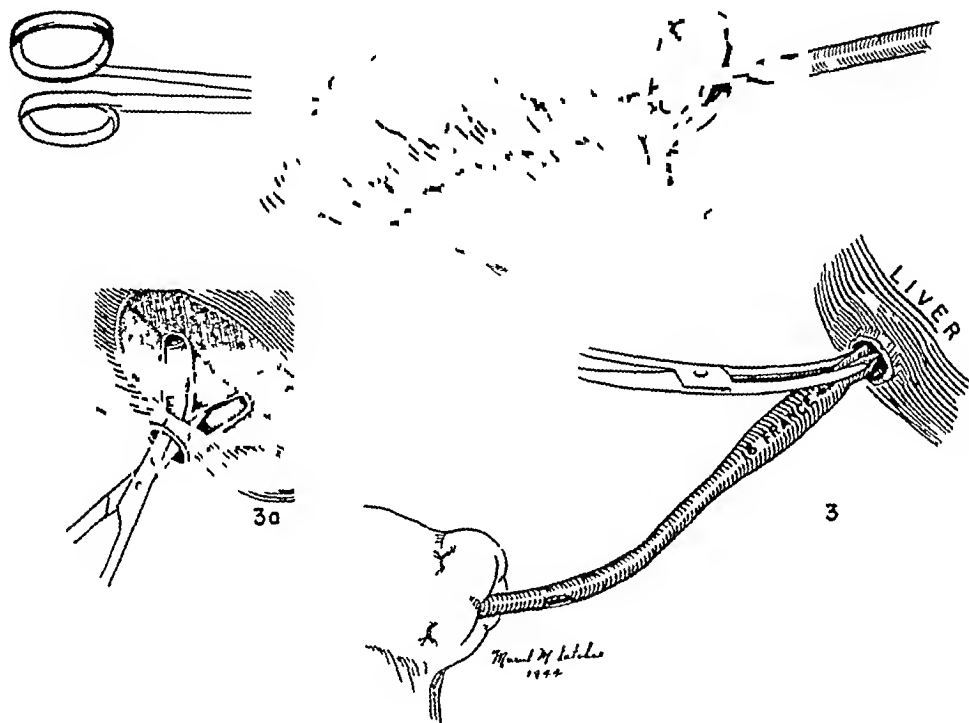


FIG 3

FIG 2—Schematic drawing to illustrate the turned in distal segment of the jejunum and how the catheter is brought down through the lumen of the intestine.

FIG 3a—Illustrates a method used in three instances to increase the depth of the hepatic duct so that at least 1 cm. of the bell end of the catheter could be held into the remaining segment of the duct. Note the eye cut in the catheter to allow bile to seep into the intestine instead of all coming through the tube to the outside.

FIG 3—Illustrates the method of introducing the bell end of the catheter into the developed segment of the hepatic duct.

under certain circumstances. This has been observed in spontaneous fistula as well as in artificial connections, when an opaque medium is seen under the fluoroscope to leave the gastro-intestinal tract and outline the hepatic duct system. That irritating substances as well as bacteria may accompany such material is easy to understand. Disabling symptoms associated with mild jaundice, fever, and chills not always occurs under these conditions. Mild cholangitis with little subjective or objective symptoms and signs may occur under all abnormal circumstances. Some such patients have little disability from these mild episodes and are doubtless included in those reported as completely relieved. On the other hand, many of them are temporarily invalided with each recurrence and finally develop continued jaundice, which varies somewhat in intensity with each acute flare. Under

rest, diet, cholagogues, *etc*, a regimen may be worked out to prevent hemorrhagic tendencies and a modicum of comfort. These victims are too often relegated to an incomplete life and early death on the basis of liver damage. In these patients, we do not always find adequate proof of ascending infection as the important factor in producing recurring attacks of cholangitis. More often, a constricted area preventing free flow of bile into the intestinal tract is the chief cause of difficulty. It is quite likely that we will find that such individuals can be cured by an operation

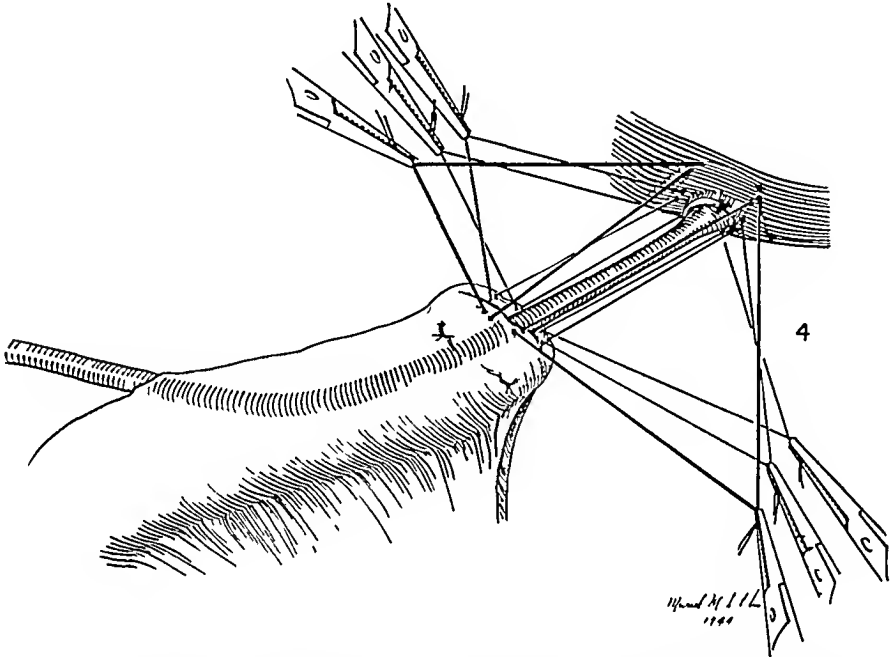


FIG 4—Schematic representation of sutures of No. 30 cotton thread placed through the scar tissue in the liver sulcus and through the jejunum. The bell end of the catheter has been fastened to the stump of the hepatic duct by two plain catgut sutures.

that does not in itself permit gradual scar-tissue obstruction. In all of these patients, we find a narrow communication between the biliary system and the intestine with inspissated bile or actual stones above it, contributing to the inflammatory symptoms observed.

All of the successful operations to restore continuity between the biliary and gastro-intestinal systems are based on a wide, free, permanent communication. The first operations were not successful because stricture eventually took place. In 1905, W. J. Mayo¹² reported a method of accurate mucosal anastomosis between the bile duct and the duodenum. Illustrations showed that a valve-like flap of duodenum was attempted. This operation has been performed extensively by Walters,¹³ with good results in at least 50 per cent of the cases. Many other surgeons have tried it with about the same percentage of cures. That this operation has not been completely successful is evidenced by the large number of plastic procedures recorded that appeared to be more rational.

Williams¹⁴ successfully implanted an external biliary fistula into the

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duodenum of a boy, age four. This fistula had been made in the early weeks of life for congenital atresia of the bile ducts. This patient has been recently seen and is in good health 30 years after his reconstructive operation. This case led to many attempts to solve this problem in adults in this manner. Most of them failed and cicatricial obstruction resulted, due to the fact that the fistulous tract had not spontaneously become lined with tissue resembling normal mucosa. The operation of Wilson, who advocated

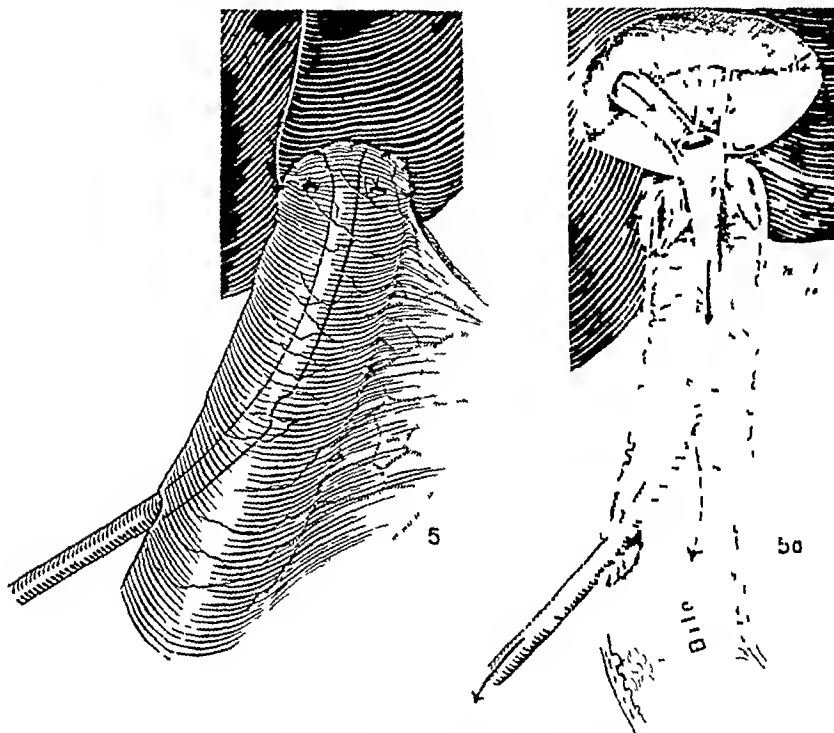


FIG 5—Illustrates the appearance of the jejunum after the sutures to the liver surface have been tied

FIG 5a—Schematic representation of the approximate appearance of the tube in situ

making a serous-lined tube from the stomach, seemed a logical step and yet we found it unsuccessful for reasons hard to explain. Dragstedt⁷ advocated the use of the duodenal wall, much as Wilson had used the stomach, and had one successful case to report. Dragstedt,¹⁵ however, has given what I believe to be important light on the subject from his work on the management of the pancreatic duct by intubation in operations requiring removal of the head of the pancreas. Sir James Walton⁶ illustrates a plastic operation using a flap of duodenal wall. Procedures such as Wilms¹⁶ and Sullivan¹⁷ proposed of using an omental graft around a tube are obviously doomed to failure in most instances.

Whatever method is adopted, one must consider the following points:

- 1 The elimination of scar tissue and preventing of its recurrence at the anastomosis
- 2 To make the anastomosis iso peristaltic with the gastro-intestinal tract
- 3 Nonabsorbable interrupted sutures should be used
- 4 Water-tight closure at the anastomosis is desirable
- 5 The anastomosis should be temporarily held open by a tube

Research along these lines, beginning in 1937, has been interrupted by propositions that seemed logical and easier than the one I am to report. Thus, Wilson's method and modifications of it were tried in the interim. The most significant change in principle came about through the vitallium tubes, as proposed by Pearse³. This appealed to me as the probable answer to the problem, and it was only after considerable trial on my own part, with

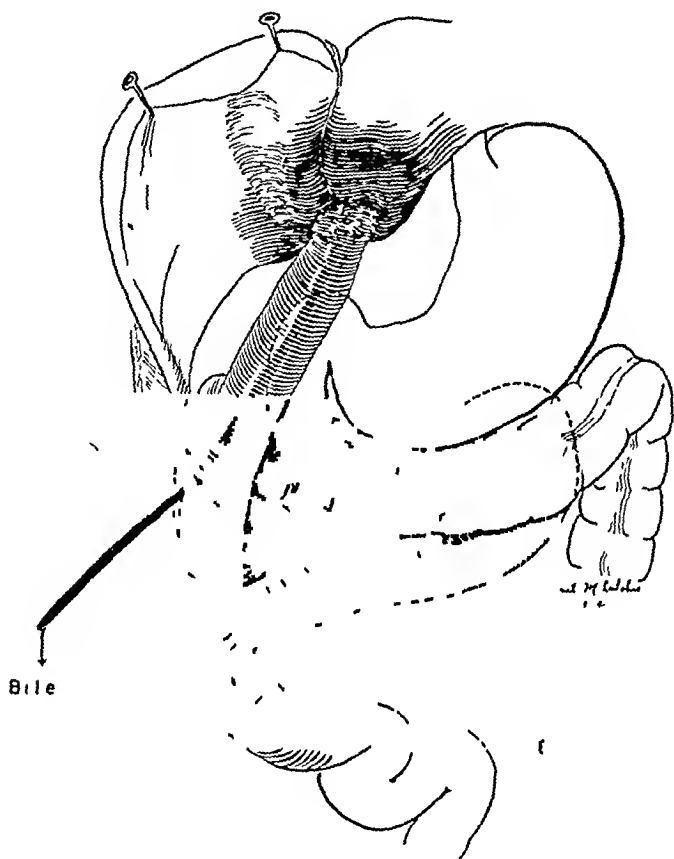


FIG 6—Schematic representation of the finished operation. The proximal end of the jejunum has been reimplanted into the side of the distal end at a low level, and the tube in the hepatic duct brought out through an omental tab, and a stab wound in the abdominal wall lateral to the incision.

the removal of several of these tubes inserted by myself and others, that I came to realize that this method had its limitations. Theoretically, it should work since there is the establishment of a more normal relationship between the ducts and the intestine. Actually, there is always a temporary respite. Bile salts do finally become deposited within the tube and thus gradual interference with bile-flow does occur with frequency. With the use of a permanent tube, one is faced with the impossibility of any dilatation of the duct. This in itself is abnormal, since the ducts have a natural tendency to dilate and thus partially take over the function of the gallbladder. Also, it is difficult to prevent the tube from passing down the intestinal tract if one end is left free in the lumen of the gut. Bile salts, administered freely postoperatively, are helpful in keeping the tube clear but have not been entirely effective in my experience. This rigid tube is of value in bridging

an unresectable area of primary carcinoma of the bile duct One such patient of mine lived nearly two years, for the most part in comfort, under these circumstances

METHODS OF REPAIR

As I have intimated in the foregoing paragraphs, it is desirable to anastomose the cut-ends of the ducts by direct suture This is applicable only to interruption by division or to a small suitably situated constriction Anastomosis may be possible months after injury since the distal segment often maintains a normal diameter When there has been the loss of a considerable portion of the duct, it is not worth while to attempt to bridge the gap by any artificial means Sutures under tension or of absorbable material are very likely to fail One can often prophesy that the result will be unsatisfactory from the prolonged leakage of bile to the outside when a poor anastomosis has been made Repair by second-intention healing will invariably result in gradual cicatricial occlusion in the region of the suture line

When there is gradual occlusion of the duct, one may expect that the distal segment will become fibrosed, resulting in little or no lumen It is unreasonable to expect that this segment can be modified in any way to form the basis of a successful reconstruction Thus, in all cases in Group 2 and in those in Group 1 with too much duct missing, one must resort to a logical procedure that fulfills the five principles of duct repair that I have set down That many of the already proposed plans will give a satisfactory result in a certain percentage of cases is admitted I have had so many failures and attempted to correct so many unsuccessful procedures undertaken by others that I have come to the conclusion that the method I wish to present may prove to be the most satisfactory I have so far tried

In eight instances now, I have developed the short segment of hepatic duct in the liver sulcus and anastomosed the open distal end of the transected jejunum to the liver around a tube placed into the duct Intestinal continuity is reestablished by implanting the proximal segment of jejunum into the distal segment after the method of Roux This results in a mechanical arrangement whereby the intestinal current is directed away from the liver Cotton or silk sutures hold the end of the jejunum securely in the liver sulcus since the scar tissue around the duct opening is very firm and reliable By inverting the end of the jejunum for a distance of 1.5 cm, we have an opportunity to place in apposition two surfaces that, theoretically at least, have healing properties One may question the fact that a small stump of duct whittled out of scar tissue will have any serosal coat remaining By the use of the bell end of a live rubber catheter, one can expect to lead all bile through such a tube and thus produce a water-tight anastomosis By making a vent in that segment of the catheter to remain for a time within the lumen of the gut, we can prevent a complete external fistula for as long as we leave the catheter in place I have experimented with leaving

the tube *in situ* for variable periods of time. One would like to get rid of it early so that all the bile would flow into the jejunum. On the other hand, it is well known that tubes removed too early may be responsible for early scar tissue constriction. This has made it mandatory in many other types of reconstruction to leave the tube in place for a long period of time, *i e*, several months. This is practical in some repairs as is borne out by the better results obtained under these circumstances. The tube is supposed to keep the anastomosis open until healing is complete and the result of inflammation replaced by more normal tissue. In our cases, we feel that leaving the tube for a long time might result in some pressure necrosis of the duct lining. For this reason, the caliber of the tube used within the duct segment is carefully selected. The majority of our tubes have been removed at the end of 21 days. This is a compromise and we may find reasons for shortening or lengthening this period of time.

In none of the eight cases has there been any bile leakage about the anastomosis. In three additional patients with huge common ducts, due to obstruction in the head of the pancreas, in whom we used the general principles of the above technic, we thought some leakage might occur but our suture lines, being placed in structures more nearly of the same diameter, were as leak-proof as those in the average case. It would be unwise, however, to fail to provide for external drainage from the subhepatic space of Morrison, since in all of these cases there is a certain amount of serous weeping due to the separation of so much scar tissue.

Three of our patients have had one or two mild transient episodes of pain, jaundice, chills and fever. These have quickly cleared and they are, on the whole, a more satisfactory group than any we have observed save those who could be subjected to an accurate end-to-end anastomosis. The longest period of observation is two years. In spite of the small number of cases and the short follow-up period, we believe that this method will be more likely to succeed in properly selected cases than any previously advocated. Although occasion has not arisen in our experience necessitating the establishment of continuity between the separated right and left hepatic ducts and the intestine, we believe that this method could be adapted under these circumstances by using two tubes instead of one.

This general principle of anastomosis of the bile duct to the end of the duodenum or the jejunum is becoming the most popular method in the one-stage Whipple¹⁸ operation for carcinoma of the head of the pancreas. When the gallbladder is used for anastomosis and the common bile duct tied, failure may result because the end of the duct often will not remain closed. Cattell¹⁹ logically advises inversion of the cut-end of the duct as one would do in the gastro-intestinal tract when a two-stage procedure makes cholecyst-jejunostomy a justifiable first-stage operation.

Since recurring attacks of cholangitis are prone to take place if permanent lateral anastomosis between the gallbladder and gastro-intestinal tract are made, I prefer as a first stage the following method. The gallbladder is

drained externally by a rubber tube brought out through a right lateral stab wound. A jejunostomy is established 50 cm from the ligament of Treitz with a No. 16 French whistle-tip catheter by a purse-string technic and brought out through a left-sided stab wound.²⁰ By elevating the cholecystostomy tube to a suitable level, after ascertaining the approximate intra-ductal pressure, one may decompress the liver more gradually. The bile is returned to the intestinal tract through the jejunostomy tube. At first this is done by a gravity bottle and later by a glass connection between the two tubes. This allows the second stage to proceed with less handicaps than encountered following any of the first stage procedures I have so far used. One may need to dismantle the jejunostomy at the second stage, which does not complicate the operation materially. The chief advantage is the ability to carry out the second stage after liver decompression in much the same manner as the universally preferred one-stage procedure.

SUMMARY AND CONCLUSIONS

Injuries to the common and hepatic ducts occur with greater frequency than is usually admitted. Many of these technical errors are unrecognized as the cause of death. Survivors are often doomed to repeated operations and a shortened life of invalidism.

No effort should be spared to teach a greater respect for the gallbladder region. Accurate identification of structures to be divided is imperative.

Early recognition of an injured bile duct is essential. Bile peritonitis is not difficult to diagnose and if treated promptly will save life or at least a dangerously prolonged postoperative course. This feature alone has made it difficult for many surgeons of vast experience to close the abdomen without drainage after operations upon the biliary system.

Prolonged external biliary fistula as well as prolonged partial or total biliary obstruction produces a life of invalidism.

Victims of partial continuous jaundice, with repeated flares of cholangitis, should not be denied further attempts for improvement by surgery. They should not be considered as invalided on the basis of unremediable biliary cirrhosis. Marked improvement and apparent complete recovery from liver damage can be brought about by providing for free flow of bile into the intestine.

Repair of the common bile duct by direct end-to-end suture is the method of choice, when feasible.

Conditions that have destroyed sufficient distal duct to make end-to-end suture impractical are most satisfactorily managed, at this time, by us by anastomosis of the remaining proximal duct to the end of the jejunum as outlined in this preliminary report.

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PRIMARY CARCINOMA OF THE GALLBLADDER*

AN ADDITIONAL REASON FOR EARLY REMOVAL OF THE CALCULOUS GALLBLADDER

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IN MANY WAYS it seems hardly worth while to offer a paper on such a surgically hopeless condition as carcinoma of the gallbladder. On the other hand, and paradoxically, that is the very reason we have the temerity to do so. Because it has such a bad prognosis once it has become established, is there anything that we can or should do to prevent its occurrence? We believe that the situation might definitely be helped in two ways. First, by stressing the fact that primary carcinoma of the gallbladder is much more common than most doctors, particularly the general practitioners, realize, and secondly, that, in a very large majority of instances, it develops as a relatively late sequela to a long-standing chronic cholecystitis and cholelithiasis. Any solution to the problem, then, would seem to lie in the realm of education, education of the doctor, from his medical school days on, in the many dangers of chronic gallbladder disease and gallstones even though *apparently* symptomless, of which the possibility of malignant degeneration is only one, and education of the public that there is only one treatment for gallbladder disease and gallstones, when their existence is proved, and that is operative removal, and the sooner the better. Most of you here hold teaching positions in some medical school. We would indeed be presumptuous to imply that we should teach you, but we do bespeak your aid in teaching others, we feel that all too frequently too little emphasis is given to the importance of operative treatment of the so-called "symptomless gallbladder" or "quiescent gallstone" until far-reaching systemic damage has been done, which is irreparable, then, by late operation. There has been a tremendous amount of discussion in recent years of the complicated operative technic for the treatment of carcinoma of the ampulla and head of the pancreas, but comparatively little has been said about the much less spectacular cholecystectomy to *prevent* the equally common primary carcinoma of the gallbladder, as well as a train of other concomitant and ultimately fatal systemic complications.

The senior author of this paper has had forcibly impressed on him the fact that carcinoma of the gallbladder is more common than is usually represented by having had among his personal cases in the ten years from 1932 to 1941, 11 patients with this affliction. It is one thing, statistically, to analyze this disease and another to observe the decline and sufferings of a fellow human being, realizing that perhaps this could have been prevented.

With this in mind we wish to reiterate the points made by numerous

* Read before the Fifty-sixth Annual Session, Southern Surgical Association, December 5-7, 1944, Hot Springs, Va

authors in recent years, that cholelithiasis is a potentially dangerous condition and that "silent stones" is a deceiving term. Among the medical profession in general there seems to be a curious reluctance regarding surgical therapy of cholelithiasis and chronic cholecystitis, until the patient himself precipitates the decision by an acute episode which does not subside under treatment with ice-caps, antispasmodics, and opiates. Every surgeon is familiar with the attitude of many a family physician or internist towards his wards as he watches them through subacute attacks of gallbladder trouble or allays the fears of the patient when gallstones are found roentgenologically or during some unrelated operative procedure. This is a most unfortunate circumstance for each such man will not observe many cases of malignancy in his own experience and thus will tend to discount his occasional patient who has a carcinoma of the gallbladder. It is the abdominal surgeon who sees most of these cases and it should be a moral obligation of his to know the facts and to urge early operation.

There are other excellent reasons that call for early operation, the most fundamental of which may be summed up in a statement of Lahey¹ "It is definitely my conviction that if patients were submitted to cholecystectomy before they had been through repeated attacks of gallstone colic, not only would the end-results be infinitely better but mortality markedly lower—Not only will early operation for gallstone be associated with a low mortality rate, but it will definitely preserve function and normal conditions in the biliary tract."

We stress also the occasional reference in the literature² to the eventual production of myocardial weakness by chronic gallbladder disease. This sequence has often been called to our attention by clinicians of wide experience. That this is no idle statement is illustrated by the fact that in the causes of hospital deaths in the 1940 series of biliary tract surgery at the Mayo Clinic, cardiovascular disease ranks first, having caused 32.1 per cent of the total mortality.³ This is a tangible factor which should affect one's decision in favor of early operation. Recent observations have also shown striking correlation between gallbladder disease and coronary artery disease,⁴ though it must be mentioned that this may be due to a basic underlying metabolic factor, as may be the case in myocardial disease.

There are other conditions which will not be elaborated upon, but which have been noted and recorded, from time to time, as resulting from calculus and infected gallbladders, such as functional gastro-intestinal symptoms, intestinal obstructions due to gallstones, arthritis, asthma, *etc.*, all with a more than presumptive cause and effect basis. Indeed, the silent gallstone is a very questionable entity.

STATISTICAL SURVEY

Admittedly, surgical statistics regarding the occurrence of carcinoma of the gallbladder are misleading. Autopsy findings are more reliable, generally speaking. Mohardt,⁵ in a recent collective review, and Kirshbaum and

Kozoll⁶ have presented large series showing that the general incidence of gallbladder carcinoma is from one-quarter to three-quarters of 1 per cent of all autopsies, or about 5 per cent of the total of all cancer disclosed at autopsy. Eight to 10 per cent of all cancer occurring in the female is primary in the gallbladder, as compared to the male incidence of 1 to 4 per cent. This discrepancy is not so striking, however, when one recalls that the occurrence of gallstones in women over 50 is about 14 per cent, but only 6 per cent in men, maintaining approximately the same sex ratio.

Primary cancer of the gallbladder is very rare in the young, there being only a few cases reported in the literature under 30 years, the youngest 22 years of age. The majority are between 60 and 70 years of age.

About 75 to 80 per cent of all carcinomatous gallbladders are found at autopsy to have coexisting cholelithiasis. Surgical pathologic reports may well show less than this, for, as we have found, inoperable malignancies cannot be satisfactorily explored for stones at the operating table. It may also be noted that in carcinoma of the biliary tract, exclusive of the gallbladder, about one-third of the cases are associated with stones.

This brings us to the fact that, statistically, we are shown that between 4 and 5 per cent of all calculous gallbladders may eventually be associated with malignancy of that organ.

Now, what kind of mortality rate do we have in prophylactic removal of symptomless gallbladders? That is difficult to determine for mortality rates presented in the literature for cholecystectomy include mostly patients in whom symptoms have demanded operation. Graham⁷ gives a rate of 1.5 per cent, the Mayo Clinic, in the 1940 report,⁸ for cholecystectomy performed for a chronic cholecystitis with stones gives a 1.6 per cent of hospital deaths. Of this last group, 7 per cent were jaundiced. Thus, we see that on a purely statistical basis, regarding the possibility of malignancy as the only reason for advising cholecystectomy, we are entirely justified in our stand, by a mortality expectancy of 1.5 to 2 per cent as against a malignancy expectancy of 4 to 5 per cent.

TABLE I
PATIENTS' AGE AT TIME OF DIAGNOSIS

40-49 years	1
50-59 years	3
60-69 years	6
70-79 years	7
80-89 years	1

Average age 67.4 years

Of the 18 cases which we are reporting in our series, two were males, 16 were females. As to age, one was in the 40's, three in the 50's, six in the 60's, seven in the 70's, and one in the 80's. The average age was approximately 67.4 years. The presence of stones was proved in 11 cases, in seven it was impossible to say, due to the extent of the growth. In 13 cases there was a history at least suggestive of gallstones for from one to over 20 years preceding the operation. In four other cases, giving symp-

toms of less than one year's duration, in every instance the complaint seemed based on already inoperable growth. In one case the history was so indefinite as to preclude any estimate of the duration of disease. In two cases there had been previous operations for the removal of stones, with drainage of the gallbladder, one, 20 years, and the other five years before the operation at which the malignancy was found. In each of these, the growth not only involved the gallbladder and adjacent liver, but also proceeded up the old drain tract into the abdominal wall. In both

TABLE II

DURATION OF SYMPTOMS SUGGESTIVE OF GALLBLADDER DISEASE

20 years or over	2
10-20 years	2
5-10 years	5
1-5 years	4
Less than 1 year	4
History too indefinite to determine	1

TABLE III

SURVIVAL AFTER OPERATION DETERMINING DIAGNOSIS

Less than 1 month	6
1-3 months	3
4-6 months	4
7-12 months	2
13-18 months	2
Over 2 years (25 months)	1
Less than 6 months—13	Less than 1 year—15

TABLE IV

PATHOLOGIC REPORT — TYPE OF GROWTH

Adenocarcinoma primary in gallbladder	6
Squamous cell carcinoma	3
Carcinoma of gallbladder primary, unspecified	7
Unsatisfactory biopsy	2

of these cases there had also been reformation of stones. Six cases survived the operation less than one month, three survived from one to three months, four from four to six months, two from seven to 12 months, two from 13 to 18 months, and one for 25 months. In three cases the gallbladder was removed. In one of these the presence of growth, in addition to stones, was suspected, but no evidence of extension beyond the limits of the gallbladder was demonstrable. This case survived 105 months. In the other two cases, very early carcinoma was found on microscopic examination, but was not suspected at the time of operation. One of these cases lived 165 months, the other 25 months, but *both died of a recurrence of the malignancy*. From this it would seem that our ability to cure already established primary carcinoma of the gallbladder by operative removal of that organ is very questionable. In a total of 1192 gallbladder operations during this ten-year period there were 18 pathologically proven cases of primary carcinoma of the gallbladder, or slightly over 1.5 per cent. This total included both calculous and noncalculous gallbladders. The percentage of cases showing primary carcinoma is considerably smaller than some other published series, but is still less than the mortality rate for this same series, which was 1.26 per cent exclusive of the carcinomas.

CARCINOMA OF GALLBLADDER

TABLE V
COMPOSITE TABLE OF ALL CASES

Patient	Sex	Age	Stones	Operation	Duration after Operation	Duration of Symptoms before Operation
M B	F	78	+	Inop *	Autopsy	Pain R U Q back and shoulder for 4 years
M W	M	74	?	Inop	4 mos	Jaundice for 6 weeks
A L	F	61	?	Inop	7 mos	Nausea, gaseous distention R U Q discomfort for 5 years
F B	F	67	+	Chole-cystectomy	25 mos	' Gallbladder trouble dating to first acute attack 20 years before
C W	F	87	+	Inop	3 days	History too vague and indefinite to estimate
J D L	F	62	+	Chole-cystectomy	16 5 mos	Acute episodes for 9 years
E M	F	57	?	Inop	5 5 mos	Attacks of gas and R U Q discomfort about 15 years
A W	M	73	+	Inop	3 mos	Gallbladder drained and stones removed 5 years previously elsewhere
W F	F	62	?	Inop	9 mos	Gas and pain in R U Q for about 1 year
E T	F	79	+	Inop	2 mos	Gallbladder drained and stones removed 20 years previously, elsewhere
A J	F	56	+	Chole-cystectomy	10 5 mos	Gas, indigestion R U Q discomfort for about 6 years
J G	F	76	+	Inop	18 days	Attacks of R U Q pain for over 2 years
E C	F	74	?	Inop	12 days (pulm emb)	Burning discomfort in "stomach for 'several years'" Rapid progression, 8 mos
A K	F	72	?	Inop	2 mos	Attacks R U Q pain for 5 to 6 years
R A	F	69	?	Inop	20 days	Pain through upper abdomen for 5 mos
D C	F	47	+	Inop	26 days (pulm emb)	Loss of weight 1 year Pain in back 3 mos
E B	F	59	+	Inop	4 mos	Anorexia and loss of weight 3 mos Pain 2 weeks
E K	F	61	+	Inop	15 mos	Pain in upper abdomen, 3 to 4 mos

* "Inop" means autopsy or exploration with biopsy of growth

DISCUSSION —From our brief series several points can be emphasized. In nearly every case the symptoms presented were due to inoperable growth, with or without preexisting symptoms of cholelithiasis. The only two cases of early carcinoma were operated upon for long-standing complaints due to the stones contained within the gallbladders, and the finding of malignancy was entirely accidental and unexpected. In spite of this, and removal of the gallbladder, both of these cases died—one in 17 months, the other in 25 months—of recurrence of the malignancy. Therefore, the result of surgery once malignancy is established is most discouraging and makes us reiterate the fact that the only hope that many of these deaths can be prevented is by early removal of simple calculous gallbladders. There are two cases included in our table which are of a group in which malignancy arose in gallbladders which had previously been drained and the stones removed. The new growth in this type of case often presents itself along the old drainage tract as it did in both of these instances. This brings up the point, that the mere removal of stones does not satisfy the moral obligation of the surgeon, removal of the gallbladder is necessary where possible.

Histopathologically, adenocarcinoma predominates, squamous cell carcinoma, usually anaplastic, is less common. Scirrhous growths are frequent, and the colloid type, with peritoneal extensions, are occasional.

In reading most reports concerning carcinoma of the gallbladder from

the surgical point of view, we have found a great deal of superfluous material, specifically in evaluation of the symptoms presented, and the laboratory findings. A simple understanding of the anatomy and pathology involved will be of most help to the clinician. Most new growths originate in either the neck or fundus of the organ. Extension is by local infiltration of the gallbladder wall then into the liver and adjacent tissues and by lymphatics to the cystic nodes, then to the nodes about the common duct.

Distant metastases are rare but may occur. The liver is usually already involved at operation.

Thus, we see that obstruction of any point of the biliary tract may occur or there may be only local extension or peritoneal implants. Due to obstruction of the cystic duct, either by stone or growth, empyema and hydrops may occur in conjunction with the malignancy.

With this simple basis of knowledge of the origin and manner of spread of carcinoma of the gallbladder in mind, it is easy to see why there is no syndrome that will make an early diagnosis possible. We have diagnosed this condition preoperatively and diagnosed patients dying without operation, but the diagnosis was based on symptoms arising as a rule from the extensive spread of the disease and other evidence of carcinomatosis. Early malignancies are found by accident, the symptoms indicating operation being due to the coexisting cholelithiasis. It is the occasional case of early carcinoma that makes us feel most futile in treatment as even here the outlook is bad because of the early spread.

CONCLUSIONS

- 1 Carcinoma of the gallbladder is more common than is generally supposed
- 2 Cholelithiasis must be accepted as an etiologic factor because of its frequent association with malignancy
- 3 Preoperative diagnosis of carcinoma of the gallbladder is difficult and treatment is rarely of value
- 4 With present day surgical methods, prophylactic removal of symptomless calculous gallbladders is entirely justified in most individuals
- 5 Valid reasons other than the possibility of malignancy are presented in support of an early cholecystectomy of calculous gallbladders
- 6 A series of cases of carcinoma of the gallbladder seen in the years 1932-1941 at the Union Memorial Hospital is presented

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DISCUSSION—DR J SHELTON HORSLEY, Richmond, Va There have been many methods of attempts to reconstruct the common bile duct One of the earliest was by Sullivan, who, in 1900, described an operation in which a rubber tube or catheter was fastened to the stump of the hepatic or the remaining end of the common duct, carried into the duodenum, and covered with neighboring tissue and omentum

In 1918, I published a paper on reconstruction of the common bile duct in which the experimental work was carried out in dogs A segment of vein was turned inside out and sutured into the defect made by resecting a portion of the common duct The operation was technically successful but biologically a failure After a few months the tissues of the vein, being unaccustomed to irritation by bile, contracted and formed a complete obstruction It was then seen that it was necessary not only to have a primary mechanical union but to make a permanent channel, tissue accustomed to its environment must be used The vein was accustomed to blood, not bile

On August 13, 1921, I operated upon a patient, Mr R B D, white, age 39, who had been operated upon elsewhere, the gallbladder had been removed at one operation and later the common duct was opened for stones The patient had a recurrence, and I united the common duct, which was greatly dilated, to the duodenum He was relieved for a while, but about two years later he had more discomfort and pain, and a roentgenogram, taken on May 27, 1924, showed that some of the barium meal entered the common duct and the hepatic ducts (slide) Obviously, the common and hepatic ducts would be filled with the duodenal contents from the normal pressure there, and regurgitation into the biliary system occurred On December 31, 1924, three years and four months after the operation I performed, he was operated upon elsewhere Many adhesions and liver abscesses were found and the patient died five days after this operation This would seem to show that any communication between the common duct and the duodenum, with its great peristaltic activity, and receiving gastric material under strong pressure from the stomach, would be unwise, as it almost certainly would be followed by cholangitis

In October, 1943, Lt Col Guy Horsley and I published a method of choledochenterostomy* in which a loop of jejunum about two or three feet from its origin was united to the common duct by a rubber band and an entero-enterostomy was made between the limbs of the loop by rubber bands to bypass the choledochenterostomy and so avoid the pressure that would force the intestinal contents into the biliary tracts (slides) I have used this technic clinically, as mentioned in this paper, and have had successful cases since this paper was published

* Cholecysto-enterostomy, Choledochenterostomy and Entero-enterostomy by Means of Rubber Bands The Use of Rubber Bands in the Mikulicz Operation ANNALS OF SURGERY, 118, No 4, 558, October, 1943

DR THOMAS J ANGLE, Boston, Mass The ideal procedure for the surgical repair of a stricture of the common bile duct is one which permits bile to flow readily through the previously injured portion of the duct, and then to pass through a normally functioning sphincter of Oddi into the duodenum. We had thought that the implantation of a vitallium tube into the common duct would approximate this ideal. Continuing experience with vitallium tubes, however, has taught us that this method, like all others we have tried, has definite disadvantages and limitations.

Dr Howard Clute and I have had 10 patients in whom 12 vitallium tubes for common duct strictures have been used. For this discussion these may be divided into (1) those in which the common duct above and below the stricture could be utilized in the repair, (2) those in which the distal end of the duct could not be so used, and, (3) stricture or narrowing of the duct from chronic pancreatitis.

Seven of our patients had common duct strictures so situated that a vitallium tube could be inserted in such a way as to reestablish the continuity of the duct and to retain the function of the sphincter of Oddi. The first of these patients, operated upon in November, 1940, was reported before this Association by Dr Clute. She has remained well since (four years) except for one attack of pain and fleeting jaundice. Three others of this group have gone from six to 18 months without trouble. The remaining three, however, have had repeated attacks of pain, fever, chills and jaundice, two have had a second attempt at repair of the stricture by vitallium tubes—one with slightly better success and one a failure. The third has gone two and one-half years since operation for a completely obstructing stricture, but is now having attacks of pain, jaundice, etc.

In brief, then, of the seven patients in whom we believed vitallium tubes would be helpful, four are doing well after intervals of from six months to four years, two are still having attacks of pain and jaundice, and one has been a complete failure.

In two cases, in spite of retrograde catheterization through the duodenum, we were unable to find sufficient distal common duct to utilize in the repair. In each case we anastomosed the common hepatic duct to the duodenum over a trumpet-shaped vitallium tube placed between the common hepatic duct and the bowel. The first patient passed the tube per bowel, she has gone two years with only occasional attacks of cholangitis. In the second patient the tube remained *in situ* and all went well for three months. She then returned to the hospital because of severe gastro-intestinal bleeding, this was fatal in spite of heroic measures to control the hemorrhage. At autopsy it was found that the distal end of the vitallium tube pressing on the posterior wall of the duodenum had caused an ulcer that bled. From these two experiences we do not recommend vitallium tubes as splints to be used at the site of a choledochoduodenostomy.

In our series the last case was one of obstructive jaundice, apparently due to pressure on the common duct from a severe chronic pancreatitis. Here a very long vitallium tube was placed in the duct. He has remained well for eight months.

The use of the vitallium tubes for the repair of common duct strictures, therefore, in our hands has given us perhaps 50 per cent good results when both ends of the duct were present. They have not been helpful in choledochoduodenal anastomoses. One case with chronic pancreatitis has apparently been helped. We are concerned with the problem of why some tubes may remain in the duct for years without trouble, and others cause difficulty in a few weeks. It may well be that with Dr Allen's ingenious new method many of our problems will disappear. Certainly our experiences with vitallium tubes leave us ready for a better method of dealing with common duct strictures.

DR FRANK H LAHEY, Boston, Mass This is a very ingenious operation and it will be a helpful addition to the number of methods that we now employ. I would like particularly to make a plea about this question of strictures of the bile ducts. Strictures should be treated primarily by the surgeons who are doing gallbladder operations, that is, they should be treated in a preventive way. About two months ago I sent an article to one of the surgical journals advocating an approach to this problem that may not be entirely accepted without some criticism.

I suggested first of all that better anesthesia, wider incisions and better exposures would prevent many of these strictures because these precautions would prevent injuries to the ducts. Because we now have repaired 130 strictures of the common duct in patients who have been sent to us, in many cases with great difficulty, my suggestion in the editorial

was that if a man injures a duct he should assess his experience very critically as to whether or not he has the skill to repair it, because in the repair of injuries to the hepatic and common ducts if the remaining ducts are again injured and so used up, another repair has less chance of being successful. One of the things we have learned is that each repair that is attempted on one of these injured ducts uses up hepatic duct until it finally disappears into the substance of the liver and so makes subsequent repairs additionally difficult and uncertain of success.

One could, of course, be accused of being selfish in stating this, but you have just heard, in this paper and the discussions, three men from Boston, each representing different institutions, on this matter of strictures, and there are many other men throughout the country who have had experience with strictures, so that I feel free to make these suggestions.

Our very best results in repair of strictures of the common and hepatic ducts have been in those patients who have been sent to us after the injury, and not too long afterward, because then there is enough of the duct structures left so that a reasonable reconstruction operation is possible.

There are several things one has to learn about strictures of the common and hepatic ducts. One is that it is possible, with the fulguration apparatus and with careful dissection, to dissect a considerable length of hepatic duct out of the hilum of the liver. One also has to learn to be reasonably immunized to opening the portal vein. I have personally opened it and sutured it six times. It is a little hair-raising, but on the other hand, the pressure in the portal vein is low and with one finger in the foramen of Winslow, pressure on the vein will control it. We have successfully sutured the vein in all these cases.

In the beginning of our experience we put in some rubber tubes instead of vitallium tubes in cases of stricture of the duct because vitallium was then not available. A few of these have worked well, but we have now replaced most of them with vitallium tubes. I do not know whether or not vitallium tubes will clog as many of the rubber tubes have, but so far it seems likely that there will be less deposit of bile salts upon them, and up to the present time they have certainly been more successful than the rubber tubes.

I do not think we should give up reconstruction of the duct by the use of the vitallium tube. I by no means feel discouraged about it. Most of the strictures are reasonably high in the hepatic duct, which leaves the sphincter of Oddi intact. I much prefer a reconstruction of the bile duct with the sphincter intact than any implantation of the cut end of the duct into the intestine or implantation of the intestine into the hilum of the liver because of the danger and frequency of ascending infections when no sphincter is present.

We have learned that one of the easiest ways to find strictures of the common duct is to turn the duodenum over, find the point of entrance of the common duct into the duodenum, follow it up through the split head of the pancreas and insert a probe upward. This will usually take one straight up to the point of stricture from which the entrance to the intrahepatic portion of the hepatic duct can be found and opened.

No one can as yet say what the ultimate results will be with vitallium tubes, but when one realizes that these cases otherwise are hopeless, I am by no means sure that they will not help us in a most difficult situation.

It may be of interest to report that a golf professional in whom we put a vitallium tube a year and a half ago is now touring the winter golf tournaments, and has finished in several of them in top-flight positions.

DR ROBERT S DINSMORE, Cleveland, Ohio. I was much interested in what Doctor Allen said about the insidiousness of the symptoms of localized bile peritonitis. I have seen patients on the seventh or ninth day following operation, without symptoms or temperature rise when we see them in the morning, and within a few hours there is a high temperature and high pulse rate. We recognize that something is wrong, open the abdomen and find a huge collection of old bile. Apparently they are able to tolerate this for some time without symptoms, not even with the uncomfortable feeling Doctor Allen described.

I have been interested in how to find that stump and would like to ask: do you go to the left side or follow the liver border down? Lord Moynihan once searched for

the stump for a long time, and finally said, after two hours "From now on I am on my own time, anything under two hours I consider the patient's!"

DR HARVEY B. STONE, Baltimore, Md. I want to say a word of commendation for the splendid paper of Doctor Finney—splendid in presentation and in the ideas it contains. I would like also to say this. At least in the community where Doctor Finney and I work, there is still a very widespread feeling among the general profession, and to a certain extent among surgeons, that there is no particular reason to be anxious about the so-called silent gallstones. He brought out many points of interest, but I think the one he emphasized particularly was that the presence of silent gallstones for many reasons should not be considered an innocuous condition, among those reasons being the close correlation between the origin of malignancy and the presence of gallstones. So I think he has given us another cogent reason why we should regard a gallbladder containing stones a menace to the patient's health, irrespective of whether or not he is suffering from it.

DR JOHN J. MORTON, Rochester, N. Y. I am sure Doctor Herman Pearce would appreciate it if anyone who has had results with the use of vitalium tubes would let him know. He is especially interested in this and attempted to review it last fall. He reported his results at the Connecticut State Medical Meeting in the fall and if I remember his figures, 80 per cent of his cases were doing very well, and there were very few reports from outside of unsatisfactory results. So I am sure he would be interested in hearing about the bad results. In his hands the results have been satisfactory, especially in those cases where there are large segments of the common duct missing.

I am glad that Doctor Allen has made this contribution, which is anatomic and gives an opportunity to use normal structures. I do not believe that turning the jejunum around will prevent ascending infection. In cases of resection of the pancreas for carcinoma, where a similar anastomosis has been used, we have seen hepatitis at post-mortem examination. This is an ever present danger when the bowel is anastomosed to the liver bile ducts or gallbladder.

DR ARTHUR W. ALLEN, Boston, Mass. (closing). Most of the queries raised by the discussors are considered in the body of the paper. Therefore, I will not repeat the reasons why I think the tube should be a temporary one and should be removable, nor why I think a rigid tube of metal not so good as one made from the patient's own tissues.

I expect that we will get less cholangitis in this low implantation of the proximal jejunum than we do in the high implantation of the stomach into the jejunum following the Whipple operation. This may not eventually prove to be true, but it now appears that these patients upon whom I have performed these operations are having less evidence of ascending infection than others have had following resection of the head of the pancreas.

Doctor Dinsmore has asked two difficult questions and I doubt if I can answer them satisfactorily. I believe that the patient who does well for seven or eight days following cholecystectomy, and then suddenly over a period of 12 hours becomes very ill with obvious peritonitis, may be explained on the basis that the ligature on the cystic duct has cut through, allowing bile to drain into the peritoneal cavity from this source. Theoretically, one should invert the cystic duct as one does the intestine when a tight closure is expected. This is not usually practical, due to its small caliber. One may have less tendency for lack of proper healing of the duct if it is crushed with a clamp before the ligature is applied. A transfixion suture distal to the ligature may prevent the tie from slipping off the duct.

The only rule I have for finding the stump of the bile duct is to follow the under surface of the liver, which I believe should be freed entirely on the right and left sides of the liver sulcus. After this is done, one usually comes down onto the portal structures which can be identified by the pulsation of the hepatic artery. Aspiration of the likely area where the duct is expected with a fine hypodermic needle, as suggested years ago by Dr. Donald Balfour, is a very useful procedure. I think it is fair to say that one should be able to expose the duct within a two hour period. Many of them are easier than others, depending on the grade and type and vascularity of the adhesions. One should not try to operate against time when doing this type of operation.

A NONSUTURE METHOD OF BLOOD VESSEL ANASTOMOSIS[†]

REVIEW OF EXPERIMENTAL STUDY REPORT OF CLINICAL CASES

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WE BEGAN AN INVESTIGATION in the early spring of 1942, seeking an efficient method of blood vessel anastomosis adaptable to war use. An early start seemed timely because it would permit an opportunity for the indoctrination of those few basic principles of blood vessel surgery so necessary to the success of any method of blood vessel anastomosis, however simple it be in technical execution.

We entered this war equipped with important adjuncts in the salvage of wounded extremities with main artery damage. The early and effective treatment for shock, the control of infection and vasospasm are known to promote the maximum blood carrying capacity of undamaged collateral blood vessels. It would be reasonable to expect, then, in this war, that extremities would survive or become gangrenous following ligation of damaged main arteries in direct accordance with the number of collateral vessels remaining anatomically intact.

It has long been known that war missiles causing damage to main arteries cause concomitant damage to collateral vessels, severe or slight, in accordance with the type of acting missile. Our first real experience with high explosive warfare was in World War I. We are informed that the shrapnel of World War I fame caused wounds characteristically destructive of collateral vessels^{1,2}. A great expansion in design of high explosive missiles in the form of land mines, grenades, fragmentation shells, aerial bombs, rocket shells, *etc.*, made it seem likely there would be a preponderance of wounds highly destructive of collateral blood vessels in this war. In view of these prospects and the fact that there is an anatomic limit to the number of collateral blood vessels that can be destroyed and yet have a limb survive ligation of the damaged main artery, the desirability of gaining control of blood flow by anastomosis in this war was early emphasized.

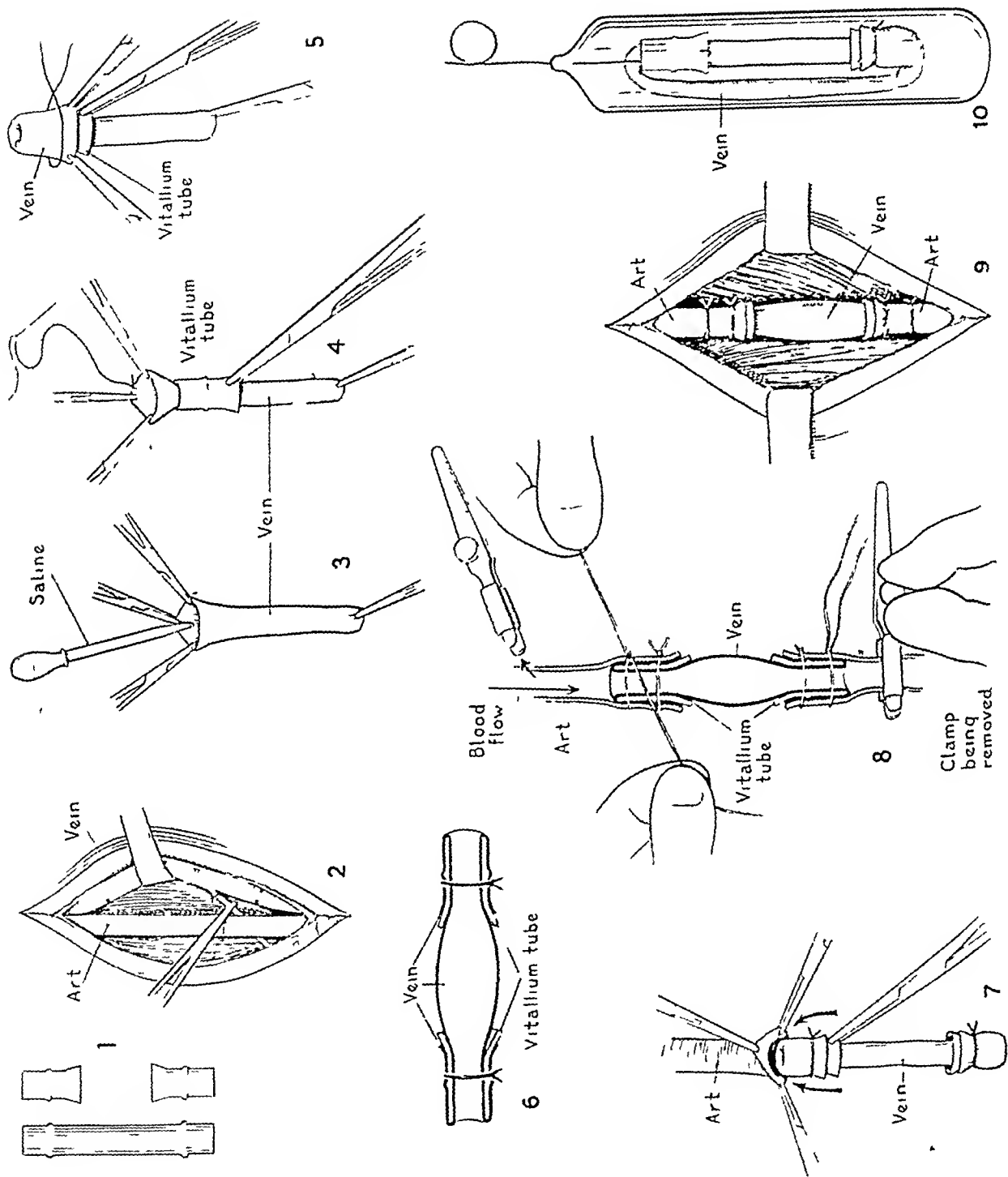
A NONSUTURE METHOD OF BLOOD VESSEL ANASTOMOSIS³

Starting with the ancient method of restoring blood flow through severed arteries, of which there is none simpler than tying the cut ends of a vessel over the ends of a connecting cannula, we added the principle of lining the cannula with a vein graft.

We selected vitallium, an alloy^{*} because of its nonirritating qualities, as

^{*} Approximate composition is cobalt 65 per cent, chromium 30 per cent, molybdenum 5 per cent. The cannulae and tubes were supplied by the Austenal Laboratories, Inc., of Chicago and New York.

[†]Read before the Fifty-sixth Annual Session, Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.



a suitable material from which to make cannulae or tubes. To facilitate bridging arterial defects of any length we recommend an identical technic employing a vitallium tube on each end of the vein graft.

Figure 1 illustrates the technic. The ends of the vein graft are everted (cuffed) over the ends of the cannula or tubes and secured by fine silk ligatures placed behind tying ridges four or more millimeters from the ends. The cut-ends of the artery are triangulated with mosquito clamps and brought over the vein-covered ends of the cannula or tubes and secured by ligatures of heavy silk placed behind the tying ridges. To prevent blood from passing between the vein and artery intimas, a fine silk ligature is tied, just snug, one or two millimeters from the end.

The method affords a broad vein intima-to-artery intima contact for the formation of a firm junction by healing. Because of the usual widespread bacterial contamination of acute traumatic vascular injuries we compared the efficiency of the nonsuture double vitallium tube technic with the Carrel suture method in vein graft bridging of femoral artery defects in contaminated wounds of dogs. The results in two series of 24-hour-old wounds, using the Carrel suture technic in one and the nonsuture method in the other, were 40 per cent successes with the Carrel suture method, as against 85 per cent successes in the nonsuture series. Débridement and the sulfonamides were used in both series and anticoagulants in neither.

At the suggestion of Dr. Rudolph Matas we investigated the use of heteroplastic vein grafts and methods of preserving them. There is clinical⁴ and experimental⁷ evidence to show that if an anastomosed main artery can be kept patent in a wounded extremity beyond the period of posttraumatic edema up to 14 days, the extremity will be saved. By that time collateral vessels will have developed sufficiently to avoid the occurrence of gangrene.

To gain information on whether heteroplastic veins will function adequately to prevent gangrene when used to bridge arterial defects the following experiments were performed. Figure 2 is a photograph of two dogs in which the right hind leg was amputated, midthigh level. After an interval of 24 hours, the legs were reimplanted, using the nonsuture two-tube technic, and vein grafts from a third and fourth animal to bridge the defects in the femoral artery and vein. The amputated limbs were preserved during the

FIG. 1.—Illustrating the operative technic of the nonsuture method. 1. Cannula and tubes (for use in the single or double tube technics). 2. Illustrates removal of vein graft. Note the branch is tied close to the vein with fine silk before clamping. 3. Irrigation of vein graft with normal saline to which a small amount of heparin may be added if desired. 4. Method of triangulating end of vein with mosquito clamps. 5. Cuffing and securing everted end of vein upon the vitallium tube. 6. Illustrates double tube technic with the vein graft mounted. 7. Introducing the distal end of the vein graft mounted upon a vitallium tube into the proximal end of the artery. 8. Illustrates tying fine silk ligatures, just snug, to prevent blood from penetrating between the vein and artery intimas. Also releasing the proximal rubber shod clamp first to facilitate the passage distalward of any residual air bubbles within the graft. 9. Completed anastomosis.—The perivascular tissues are closed snugly around the anastomosed artery when possible. 10. A convenient way of preserving, hermetically sealed in an ordinary test tube, a vein graft for quick freezing. The graft is moistened with normal saline, one end mounted upon a vitallium tube in the usual manner, the other end is passed through a second tube and brought over the first tube to protect the intima until used. A wire serves to suspend the graft.

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24-hour interval in cracked ice. The dogs were given sulfathiazole, one gram twice daily from the time of the first operation. The photographs were made 12 and 21 days, respectively, following reimplantation of the limbs, and there is every evidence of a good supply of arterial blood in these reimplanted limbs. Heteroplastic vein grafts were used to bridge femoral artery defects in ten additional animals. The anastomoses functioned for 27 days (average), which is well beyond the postulated 14 days of posttraumatic edema.



FIG 2—Photograph of two dogs, No 2110 (12 days) and No 2092 (21 days) postoperatively, in which the right hind leg was amputated at the mid thigh level and reimplanted after having been kept in cracked ice for 24 hours. Moderate edema is still present in the 12 day animal.

THE PRESERVATION OF VEINS

We have found that veins quick-frozen in an alcohol dry ice mixture and kept in the frozen state function adequately when used as heteroplastic grafts to bridge arterial defects. The veins may be kept at or below minus 40°C for indefinite periods. We proved continued patency of the anastomosis in two instances at 38 days, following the use of grafts, preserved nearly three months, to bridge femoral artery defects in dogs. Patency of an anastomosis was demonstrated at 19 days following the use of a quick-frozen segment of human saphenous vein, preserved three weeks, to bridge a defect in a dog's aorta (Fig 3).

Figure 10 illustrates a convenient way of preserving a vein graft quick-frozen for emergency use. Note that one end of the vein graft is already cuffed on one vitallium tube with the other brought over it to protect the intima. Repeated demonstrations have revealed that with ready-mounted vein grafts at hand, completion of an anastomosis may be routinely accom-

plished within 15 minutes by the average operator. For war use, ready-mounted, quick-frozen, vein grafts serviced to field and evacuation hospitals *via* the blood bank personnel, would afford an important alternate, during large offensive engagements, to the necessity of having to remove grafts at the time.

We present two cases to illustrate the application of the nonsuture method of blood vessel anastomosis in the treatment of acute traumatic extremity wounds with main artery damage.



Fig 3—A photograph of a dog's aorta taken 19 days after operation. A defect in the aorta was bridged with a segment of human saphenous vein which had been preserved quick frozen for three weeks. Note the funneled ends of the two vitalium tubes and the vein graft in between.

Case 1—No 714522 M E. A seven-year-old boy admitted to P H, July 20, 1943, in shock due to hemorrhage from a severed brachial artery. The boy's left arm had been pushed through a glass door while at play. He received an irregular laceration across the inner aspect of the middle section of the arm. The brachial artery, median and ulnar nerves were severed. The patient was promptly given 500 cc of blood, 300 cc of normal saline and 2 grams of sodium sulfadiazine, intravenously.

Operation—(Five hours after injury) Ether anesthesia. A pneumatic tourniquet was applied well above the wound. The skin was carefully "prepped" and the wound thoroughly irrigated with saline. The retracted ends of the severed brachial artery were freed for a distance of 5 to 6 cm. The tourniquet was released sufficiently to flush out severed vessels. Rubber-shod clamps were quickly applied to the ends of the severed artery and the latter irrigated with saline. The cut ends of the brachial vein were transfixed with "C" Deknatel silk. As debridement proceeded, the smaller vessels were ligated with "B" Deknatel silk.

At this point of the operation the team was divided. This enabled one section to proceed with repair of the nerves, using arterial silk, while the other proceeded with preparation of a vein graft for bridging the arterial defect. Accordingly the left femoral vein was isolated for a distance of 10 cm distal to the origin of the profunda. Branches were ligated with "B" Deknatel silk flush with the vein, clamped, cut and ligated distally (Fig 1). A ligature of No 1 Deknatel silk was placed on the distal end of the femoral vein. The blood was milked upward and another ligature placed proximalward. The vein was further secured with transfexion ligatures and the intervening segment quickly removed. (The length of a vein segment before removal should be 2 cm longer than the arterial defect). The vein graft was thoroughly irrigated with

saline. A silk suture on a straight needle passed through the wall of the distal end served to pull the vein through a 2 Mm vitallium tube and later, when cut short, to identify the distal end of the vein graft. The end of the vein was everted (cuffed) over the vitallium tube and held in place by a ligature of No 1 Deknatel silk placed behind a tying (holding) ridge (Fig 1). The other end of the vein graft was mounted, in identical manner, upon a second 2 Mm vitallium tube. (Care must be taken to avoid a valve at the eversion site to prevent diaphragm occlusion.)



FIG 4—Arteriogram of the anastomosed brachial artery in Case 1, taken one month after operation. Whereas, the funneled ends of the vitallium tubes are close together, a column of diodrast may be noted passing through the intervening vein graft. Compare the long tubes as used in this case with the shorter tubes of recent design (See insert).

Next, the severed ends of the artery were debrided and again irrigated to remove clinging particles of fibrin. (Control of blood flow by the rubber-shod clamps placed well away from the ends must be absolute).

The distal end of the severed artery was then triangulated by placing mosquito clamps, taking 15 Mm bites, upon the cut edge. The flange of the vitallium tube carrying the proximal end of the vein graft was grasped with a stout, straight clamp and the graft was dipped in saline. Following this, the vein-covered tube was introduced into the funneled end of the artery and the latter brought well up on the tube. The artery was secured to the tube, intima to intima with the vein, by a No 3 Deknatel ligature tied tightly behind the holding ridge, using a surgeon's knot (Fig 1).

The second vitallium tube, bearing the distal end of the vein graft, was irrigated with saline (using a blunt nose medicine dropper) and quickly introduced into the proximal end of the artery in an identical manner. Finally, ligatures of No. 1 Deknatel silk were placed around the artery, barely snugging the artery to the cuffed vein at a point 1 to 1.5 Mm from the ends of the vitallium tubes (Fig. 1).

Just before removing the rubber-shod clamps 15 mg of heparin (15 cc of liquaemin) was injected in the artery just proximal to the anastomosis using an hypodermic needle. The proximal clamp was removed first, followed immediately by removal of the distal rubber-shod clamp. (Should this not serve to force all trapped air bubbles distally from the vein graft, elevation of the limb with gentle milking pressure upon the graft must be resorted to).

A pink color of the boy's hand resulted immediately after reestablishment of blood flow, and only a few minutes elapsed before the left hand was as warm as the right. The muscles, fascia and skin were approximated with fine silk. The patient received 300 cc of blood during the operation and left the table in excellent condition. The arm was placed in a plaster splint with the hand in volar flexion.

Postoperative Course—The wound healed per primam. The patient was discharged on the 11th postoperative day in a constant tension splint to permit exercise of unopposed extensor muscles, but protecting the paralyzed flexor muscles of the forearm against overstretching. Sulfadiazine therapy was continued through the fifth postoperative day. We cannot say that postoperative heparinization was adequate (its administration by continuous intravenous drip was discontinued after 60 hours), because the clotting time (capillary method) varied from 3 to 6 minutes. Daily observations of the left radial pulse revealed it unchanged in volume.

Follow-up 1 month Patient receiving physiotherapy. Left radial pulse remains good. Arteriogram (Fig. 4) confirms the patency of the anastomosis. However, thrombosis of the anastomosis took place immediately following the injection of diodrast.

Follow-up 5 months Chronaxie studies reveal innervation of the forearm muscles supplied by the median nerve.

Follow-up 14 months Complete sensory and motor recovery of the median and ulnar nerves. However, there is yet some inability to completely extend the fingers due to weakness of the interosseal muscles, though chronaxie studies reveal complete regeneration.

Follow-up 19 months Complete return of function.

Case 2—No. 751446 R. J. A 15-year-old colored boy entered the P. H., July 7, 1944, with a severe laceration of his left arm. He incurred the injury falling through a plate glass window. A tourniquet was promptly applied. After his arrival at the hospital, some hours later, a pneumatic tourniquet was applied, and deflated at half hour intervals. Family and past history noncontributory.

Physical Examination Temperature 101° F, pulse 132, B. P. 160/80. An apprehensive, well-developed male, not in shock. Examination of the left arm revealed a transverse laceration starting in the midbiceps region, directed obliquely downward, dividing all soft parts to the bone, and entering the elbow joints anteriorly. The laceration involved approximately two-thirds of the circumference of the arm. The radial and median nerves were severed as were the brachial artery and accompanying veins. As a result of muscle retraction the wound gaped widely. The forearm and hand remained pale, cold and pulseless following removal of the tourniquet.

Operation—The operation consisted of irrigation and débridement of the wound, suture of the radial and median nerves. The brachial artery defect was bridged with a segment of saphenous vein, using the nonsuture technic, with a 4 Mm vitallium tube on each end. Twenty milligrams of heparin (2 cc of liquaemin) was given intra-arterially upon establishing blood flow through the anastomosis. Five grams of sodium sulfadiazine was given in saline during the operation. Hemostasis was completed and the

muscles fascia and skin were sutured. Silk technic was used throughout. The arm was placed in a posterior molded plaster splint with the elbow at right angles. An excellent radial pulse was felt upon releasing the brachial artery to blood flow.

It was of extreme interest, however, that immediately following complete release of the tourniquet and restoration of flow through the anastomosis, the patient began to go into shock. The B P fell from 160/75 to 90/40 within five minutes, and was down to 55/40 during the next 30 minutes in spite of the rapid administration of 500 cc of whole blood. One hundred milligrams of eschatin was given, and the patient recovered slowly from shock. Whereas 200 mg of heparin in Pitkin's menstruum



FIG 5—Arteriogram of Case 2. Taken 34 days after operation. Note the patent saphenous vein graft is about the same size as the anastomosed brachial artery. The slight bulge of the upper end of the graft marks a valve site in the vein graft.

(Loewe method) was given subcutaneously in the lateral aspect of the thigh, it is likely that its action was neutralized in great part by subsequent transfusions of whole blood. Within one hour after the conclusion of the operation the entire arm was greatly swollen and remained so for many days. Edema was so great during the first four days a radial pulse could not be felt. Oscillometric readings, however, indicated patency of the anastomosis. The patient's temperature ranged from 103° to 104° F the first three days. A prompt fall in temperature followed a shift to penicillin therapy. The wound healed *per primum*. The radial pulse remained excellent and 34 days post-operative an arteriogram confirmed the patency of the anastomosis (Fig 5).

Follow-up 4 months Radial pulse remains excellent. Chronaxie studies revealed no innervation of the forearm muscles as yet. Muscles supplied by the tourniquet damaged ulnar respond to direct stimulation, whereas there is no response from those supplied by the sutured radial and median nerves. Furthermore, the latter muscles are more wasted and fibrotic.

Follow-up 7 months Evidence of beginning nerve regeneration.

DISCUSSION—The similarity of these wounds to war wounds was as follows: (1) Damage to collateral vessels was extensive because of the location and scope of the wounds. (2) They were contaminated wounds, with delayed treatment. Time elapsed from injury to reestablishment of blood flow by anastomosis was eight hours in both cases.

F H noncontributory P I The pulsating tumor became apparent to the patient a few days following a bullet wound His important disabilities were increased sensitiveness of the leg to cold, decreased exercise tolerance both in the leg and general, and exertional dyspnea

Physical Examination—The heart percussed large and a systolic murmur was heard over the precordium B P rt arm 110/40 Examination of the rt leg revealed a pulsating mass 5 x 3 cm over Hunter's canal at the junction of the upper and middle thirds A small scar in the overlying skin marked the entrance of the bullet A thrill was palpable over the mass and a continuous bruit with systolic accentuation could be



FIG 6A



FIG 6B

FIG 6—A & B Arteriograms of Case 3. A Shows a diodrast visualization of the arteriovenous fistula of the femoral artery and vein taken before operative excision of the fistula. Note the spasmodic narrowing of the artery proximal to, and its dilatation at, the fistula site. A segment of this hugely dilated vein was used as a graft to bridge the arterial defect following excision of the fistula. B An arteriogram 14 days after operation demonstrates the patency of the fistula. Note the small size of the intervening vein graft in comparison with A.

heard. Pulsation was faint in the rt popliteal artery and absent in the distal arteries. Obstruction to blood flow through the fistula caused marked bradycardia. A roentgenogram of the heart revealed an increase in the transverse diameter of the heart, most marked to the left. Hb 148 Gm, R B C 5,910,000.

Operation—Excision of the A V fistula, with vein graft bridging of the arterial defect by the nonsuture method, using a segment of the accompanying femoral vein. The fistula measured approximately 1 cm in diameter. Pressure closure of the fistula caused an increase (from 4 to 8 Mm) in the diameter of the distal portion of the femoral artery. Diameter of the artery proximal to the fistula approximated 12 Mm, with some thinning of the vessel wall. Upon release of the rubber-shod clamps and reestablishment of the circulation, the vein graft dilated to 2 cm, but was reduced considerably by closing the perivascular tissue snugly around it. Following the anastomosis there were excellent pulsations in the dorsalis pedis and Posterior Tibial arteries. Two weeks later, arteriography confirmed the patency of the anastomosis (Fig 6). Blood clotting time was maintained around 55 minutes for eight days following operation, using subcutaneous heparin.

Circulation studies before and after operation, using radioactive isotope sodium were as follows. Circulation time (arm to foot) of the normal (left) leg was 40

seconds compared to 30 seconds for the right leg after operation. A volume flow to the rt foot preoperatively was 40 per cent below the normal left foot whereas postoperatively the volume flow to the rt foot was increased to 20 per cent above the normal left leg. The above studies were carried out at rest.

Follow-up—Four months postoperative, slight swelling of leg upon standing for long periods which disappears quickly upon exercise. Foot on operated leg feels warmer than left foot. Plays tennis and goes deer hunting. The latter involves walking up and down mountains often as much as ten miles a day. Examination Rt foot warmer than left. Pulsation felt over anastomosis, popliteal and foot arteries. Oscillometric readings, Lower $\frac{1}{3}$ Rt = 2, L = $1\frac{1}{2}$.

COMMENT—It is an established fact that quadruple ligation, with excision of the fistula, eliminates the likelihood of recurrence in cases of traumatic arteriovenous fistula. Likewise, there is little likelihood that gangrene will follow this procedure when done two or more months after injury. All concede that the procedure eliminates the deleterious effects of the disease upon the heart. Nevertheless, though the patient may be greatly improved symptomatically following this operation, the affected extremity is rarely capable of as full exertional response as the normal extremity without the occurrence of some symptoms.

A follow-up on three cases of traumatic arteriovenous fistula of the femoral vessels treated by ligation, with excision of the fistula were as follows. One man, age 26, reports discomfort in the calf of the leg when walking as long as two years after operation. A 29-year-old man, now four years since operation, is capable of walking only two miles at a slow pace without developing leg fatigue and pain, for this reason he was discharged from the Army. The third case, a professional dancer, age 30, has not been able to resume his work because of leg symptoms, now five years since operation. In none of these cases was the individual able to indulge in the vigorous sports or exercise to which they had been accustomed before receiving their injury. To compare with these results, we cite a case of arteriovenous fistula of the popliteal vessels upon whom one of us (A. H. B.) operated upon in 1934. Patency of the parent vessels was successfully maintained in this case, with elimination of the fistula by reconstructive aneurysmorrhaphy. The young man took up professional boxing after operation and has carried on with vigorous exercise, remaining completely symptom free. Now, eight years since operation, pulsation of the arteries is equal in the two feet. There was no section of sympathetics at operation in this case.

It would seem worth while to maintain the patency of the parent artery particularly in cases of arteriovenous fistula of the leg. We believe vein graft bridging, using the nonsuture technic, will make this feasible in a great percentage of cases. This affords a chance for complete restitution of function under all exercise conditions—an important item particularly to the soldier or young man. In our case the young man's greatest ambition was to regain his laurels as an amateur skater.

A case is presented illustrating the use of the nonsuture method of blood vessel anastomosis for vein graft bridging of the arterial defect following excision of peripheral arterial aneurysms.

Case 4—No 680199 E. P. A 62-year-old colored male was admitted to P. H., August 29, 1942, complaining of a painful, pulsating swelling on the inner side of the right thigh of four weeks duration. P. H. Admits the presence of a primary lesion at age 20. P. I. Onset of the swelling on the thigh followed two weeks after a sudden muscular effort to prevent a fall.

Physical Examination A markedly arteriosclerotic individual appearing older than his years B P 158/88, heart slightly enlarged Examination of the right leg revealed a pulsating mass, 8 x 6 cm, over the region of the distal end of Hunter's canal A systolic bruit was heard over the mass Pulsation was present but diminished in the rt popliteal and foot arteries Laboratory Kline +++++ Electrocardiogram revealed left axis deviation

Operation—Excision of the aneurysm with restoration of blood flow by vein graft bridging of the arterial defect, using the nonsuture method, double vitalium tube technic The aneurysm arose at the femoropopliteal junction, and was 8 cm in diameter Thrombosis of the accompanying vein necessitated taking a segment of femoral vein from the left leg for use as a graft The anastomotic magna artery was compromised by the pressure of the aneurysm The parent artery was markedly arteriosclerotic with eggshell intimal plaques The patient had been given dicoumerol preoperatively, with the idea of combining its use with heparin so the latter could be discontinued shortly after operation A misjudgment in their use resulted in a two-hour clotting time for hours postoperatively The amount of blood given necessary to overcome this caused cardiac decompensation, with massive edema, which resulted in our inability to palpate a pulse in either leg Repeated oscillometric readings, however, revealed the anastomosis to be patent for 72 hours after operation Fortunately, by this time, collateral circulation had developed sufficiently to maintain the viability of the leg A diodrast study of the rt femoral artery two weeks after operation confirmed the thrombosis of the anastomosis and demonstrated patent collaterals

Follow-up Patient was placed on antiluetic therapy Buerger's exercises were continued because of inability to feel arterial pulsations in either foot He returned to his work four months after operation, and has worked ever since He states the right leg becomes more tired than the left on exercise Now two years after operation

COMMENT—We did not attain the ideal, namely, the restoration of a normal, pulsating volume blood flow permanently through the parent artery in this case However, the fact that the anastomosis did function for three days is, in our opinion, the reason why gangrene failed to occur following operation Whereas, the presence of numerous sclerotic intimal plaques was undoubtedly responsible for the initiation of thrombus at the site of the anastomosis in this 62-year-old man It seems likely that the diminished rate of blood flow, a result of cardiac decompensation, was a contributing factor At any rate, it is reasonable to suppose that the anticoagulant therapy may have prevented extension of the thrombus to occlude important collateral branches

It is not reasonable to expect maintained patency in the anastomosis of badly degenerated, arteriosclerotic vessels, irrespective of the method or adjuncts employed It is our opinion that the nonsuture method will attain a high percentage of successes when employed in cases of syphilitic or traumatic peripheral arterial aneurysm not complicated by severe arteriosclerosis In stating the above opinion, we hasten to caution against its indiscriminate use, however Restoration of blood flow by vein graft bridging usually necessitates preliminary excision of the aneurysm The latter procedure is far more destructive to collateral blood vessels than the operation of obliterative endo-aneurysmorrhaphy devised by Dr Rudolph Matas Therefore, the location of the aneurysm in relation to important collateral branches and other considerations in the particular case should govern the decision as to the

choice of methods, though all may agree that restoration of flow is the ideal and offers the best chance of complete restitution of function

PORTAL-CAVAL ANASTOMOSIS BY THE NONSUTURE METHOD
FOR THE RELIEF OF PORTAL HYPERTENSION

A more common cause of portal hypertension is obstruction to the flow of portal blood through the liver due to Laennec's (portal) cirrhosis. Or, cases of congestive splenomegaly (Banti's syndrome) in which the obstruction may be in the portal or splenic veins. It has long been appreciated that the successful establishment of a portal-caval shunt would have a beneficial effect upon the control of bleeding in the gastro-intestinal tract the result of portal hypertension. The technical ease with which blood vessel anastomosis may be accomplished, using the nonsuture, vitallium tube method, naturally suggested its application to this vascular problem.

With the valued cooperation and skillful aid of Dr. Allen O. Whipple we have been able to establish end-to-end anastomoses between the splenic and left renal veins following removal of the spleen and kidney in five cases. Operation upon two cases of cirrhosis has been too recent to evaluate the results.

Case 5—No. 690444. A P. A five-year-old girl of Polish parentage was first admitted to P. H. in October, 1942, with the complaint of abdominal enlargement of three months' duration. Family and past history noncontributory. Present illness. Onset with progressive enlargement of abdomen and anorexia. Mother had noticed an increasing tendency to bruise following minor traumata.

Physical Examination. The child appeared chronically ill. The pertinent findings were confined to the abdomen. The latter was protuberant, with visibly distended venous channels. There was no free peritoneal fluid. The liver was enlarged 8 cm. below the costal margin and was firm, with a sharp border. The spleen extended 10 cm. below the costal margin and was very firm. Studies revealed a moderate derangement of liver function. *Diagnosis.* Portal cirrhosis, congestive splenomegaly. The child was placed on a high protein, high vitamin diet and discharged December 1, 1942.

Readmitted to P. H. May 25, 1943. General condition unimproved. On examination, the child was markedly anemic. The liver and spleen remained enlarged as before. Three transfusions were given during the next two weeks. A stool examination was positive for blood. Though an esophagram failed to show esophageal varices on the 15th day after admission, the child began to vomit large quantities of blood. For several days blood replacement was carried out by continuous transfusion. During the ensuing month the child's condition remained desperate. Her hemoglobin could not be maintained above the low forties. The ascites that had supervened became irreversible.

Operation—July 26, 1943. The child's abdomen was explored with the hope that blood could be shunted from the portal to the caval systems by anastomosing the splenic to the renal vein, employing the nonsuture technic.

Pathology. The liver was markedly cirrhotic, the spleen eight to ten times normal in size. There was considerable collateral circulation between the splenic, gastric and omental vessels. Considerable ascitic fluid was present. The right and left kidneys appeared normal.

Procedure. A long left rectus incision was made. The spleen was mobilized. The splenic artery ligated. The splenic vein was closed by a serrefine clamp, sectioned near the spleen and the latter removed. The splenic vein was then dissected proximally for a distance of 8 cm. and irrigated with normal saline. The tail of the pancreas and the left kidney were mobilized. The renal artery and ureter were ligated and cut. The

renal vein was mobilized throughout its length. A serrefine clamp was applied proximally and the vein sectioned near the kidney.

Anastomosis The end of the splenic vein was passed through a special vitallium tube, and everted (cuffed) over the tube. The vein was held in place by a No. 1 Deknatel silk ligature tied tightly behind a holding ridge on the tube, some 5 mm from the end. The renal and splenic vein stumps were irrigated with normal saline. The vitallium tube bearing the cuffed end of the splenic vein was then introduced into the stump of the renal vein. The latter was drawn well up on the tube and secured by a No. 3 Deknatel ligature passed around the two veins over the tube and tied tightly behind the above-mentioned holding ridge. This afforded a broad splenic vein intima-to-renal vein intima contact. A second ligature of No. 1 Deknatel silk was tied, just snug, near the end of the vitallium tube (Fig. 1), to prevent blood from penetrating between the intimas. 15 mg (15 cc) of heparin (liquaemin) was given intravenously. The serrefine clamp on the splenic vein was removed quickly followed by removal of the serrefine clamp on the renal vein. Upon opening the anastomosis blood rushed through from the portal system *via* the splenic vein into the caval system *via* the renal. There was slight angulation of the splenic vein over the funnel edge of the tube.

Closure The abdomen was closed with near-and-far steel wires, the skin with interrupted silk.

Condition The patient left the table in fair condition, having received a transfusion of plasma and blood during the operation.

Postoperative Course Heparin was continued by intravenous drip for two days. On the second day she became distended, dyspneic and stuporous. The temperature rose to 104° F. Oliguria developed, and moist râles appeared throughout the lungs. The nonprotein nitrogen rose to 85 mg per cent. The exact cause of the unfavorable course was unknown, but it was felt that "hepatorenal" failure was a contributing factor. A duodenal tube was passed. Large amounts of fluid, blood and massive parenteral doses of vitamin "B" complex were given with sudden dramatic results. Kidney function improved. Nonprotein nitrogen dropped to 43 mg per cent on the fifth postoperative day, and convalescence from then on was uneventful.

Pathologic Findings Liver cells (microscopic), varying in size, were accumulated in large and small islands between wide bands of connective tissue. Spleen microscopic sections revealed the usual picture of congestive splenomegaly. Examination of the left kidney revealed numerous cysts, 0.5 to 2 mm in diameter, scattered throughout the cortex and medulla. The cysts were lined with flattened epithelium. In addition, small, wedge-shaped areas of scarring and cellular infiltration occur. In them the glomeruli are sclerotic, the tubules dilated and filled with hyaline casts. Lymphocytes predominate in the cellular exudate.

The diagnosis of congenital cystic kidney with superimposed infection was a discouraging finding in this case. However, reevaluation seven months postoperatively revealed that she had gained four pounds, had a good appetite, and played actively. There had been no recurrence of the ascites. The superficial collateral veins over the abdomen had receded markedly (Fig. 7). There was improvement in the hemoglobin (12.5 Gm), stool guaiac-negative for blood. Urine: Concentrated specimen showed many hyaline casts, few R. B. C. and W. B. C., sp. gr. 1.009, and a faint trace of albumin. N. P. N. 42.9 mg per cent, urea ratio 50.6. Phenolsulphonephthalein excretion 50 per cent. Many determinations of B. P. ranged from 110/76 to 126/80.

Reevaluation 12 months Postoperative July 17, 1944. Appetite good. Gaining in weight. No bleeding episodes, though mother states the child "bruises easily." Examination B. P. 124/76. Superficial abdominal veins not prominent. No edema or ascites. Liver edge 6 cm below costal margin. Laboratory: hemoglobin 11.3, R. B. C. 3,500,000. Urine: Sp. gr. 1.016, alb. ft. tr., microscopic shows few W. B. C. N. P. N. 46.4, urea N. 36.7, urea ratio 79.1. Total proteins 7.6. Albumin 4.08 Gm, globulin 3.53 Gm. Stool guaiac-negative for blood.

Summary of the test pertaining to the liver status before operation, 6 and 12 months after operation is as follows. No change in protein partition (Albumin and globulin ratio was never reversed). An elevated prothrombin time before operation returned to normal after operation. A three plus cephalin flocculation test and an increased bromsulphalein have surprisingly returned to normal after operation, while the galactose tolerance and hippuric acid conjugation tests have shown increased impairment.



FIG 7A

FIG 7B

FIG 7—A & B Infra red photographs of the superficial collateral veins in Case V. Photograph A was taken 26 days following the establishment of a portal-caval shunt. B was taken 15 months after the establishment of the portal-caval shunt.

The patient continued to do well until October 8, 1944, when she felt weak, dizzy, and passed three tarry stools. Her mother gave the story of a recent nosebleed. She was admitted to B. H. and given multiple transfusions over a period of eight days. The initial hemoglobin of 50 per cent rose to 82 per cent. The liver was enlarged, as before. No ascites present. Even after complete restoration of her blood volume, no increase in distension of the superficial abdominal veins was noted (Fig 7). She entered the hospital with an N. P. N. of 90, which two days later had fallen to 47.9. This was a higher N. P. N. figure than recorded during the days of the hepatorenal failure immediately after operation. The diastolic blood pressure was consistently higher on this admission and the systolic somewhat higher. During the year and three months since operation, the child has increased in height from 40.25 inches to 44.75, weight from 33 lbs to 48 lbs. She was discharged October 21, 1944, having a guaiac negative stool.

SUMMARY A five-year-old child diagnosed as portal cirrhosis who, after eight months, developed massive hemorrhages from esophageal varices and ascites. A portal-caval shunt was established following removal of the spleen and left kidney. Examination of the kidney revealed the additional diagnosis of congenital polycystic disease. The general health of the child improved markedly after operation and this improvement was maintained over a period of 15 months. There was improvement in some of the liver function tests and no return of the ascites. Frequent examinations of the kidney, however, showed gradual increased impairment. At 14 months postoperatively the child had a nosebleed, and a few days later passed a tarry stool. The blood pressure (systolic

and diastolic) averaged higher than previous levels, and the N P N was 90. She responded to transfusions and is now back at school.

Case 6—No 756752 M A A 15-year-old girl was admitted to P H, August 17, 1944, with the history of repeated massive hemorrhages into the gastro-intestinal tract since the age of four. Such attacks were characterized by tarry diarrhea and coffee ground vomitus followed by the vomiting of bright red blood. The attacks would last from one day to one week, and it had been repeatedly noticed that the spleen, which was enlarged, would shrink considerably following each episode of hemorrhage. During the past four years the patient had experienced at least four attacks, the most recent one having occurred two months prior to admission. Family and past history otherwise unremarkable.

Physical Examination—This revealed a normal-appearing girl, with the only positive finding of an enlarged spleen extending downwards to the level of the umbilicus. The liver was not enlarged and there were no prominent veins over the abdomen, nor were there evident hemorrhoids. There was no evidence of ascites. Laboratory findings of interest included evidence of esophageal varices at its lower end, normal serum protein and albumin-globulin ratio, normal bromsulphalein test, R B C of 3.9 million, Hb of 12 Gm, W B C of 4,300, and smear showed a reduced number of platelets.

Course After the establishment of normal renal function bilaterally by intravenous pyelography, the patient was operated upon on the 6th hospital day. The liver was found to be normal, and an anastomosis, using a 7-Mm vitallium tube, was established between the splenic vein and the left renal vein, following the removal of the spleen and left kidney. Measurement of the pressure in a branch of the coronary vein before the anastomosis was 310 Mm of water and following the establishment of the anastomosis it fell to 190 Mm of water. The postoperative course was uneventful, and she left the hospital on the 15th postoperative day.

Follow-up Feels well. Has gained 10 lbs. No recurrence of bleeding, now three months since operation.

Case 7—No 754188 J C, a 38-year-old male, was admitted to P H August 10, 1944, complaining of a sensation of discomfort in the left flank of seven months' duration. For two months the patient had felt weak and tired. Three weeks later he developed an acute polyarthritis, associated with fever. Improvement in the joint symptoms occurred in one week, but for the three weeks prior to admission the patient had noted dark urine and mild diarrhea. There had been no jaundice, ascites, vomiting or evidence of bleeding.

P H revealed an attack of "yellow jaundice" associated with light stools of three weeks' duration at the age of 17 years. There was no history of exposure to hepatotoxic agents.

Physical Examination—A well-developed male, without jaundice, the liver edge was 2 cm below the costal margin at the midclavicular line, and the spleen was 7-8 cm below the left costal margin. Laboratory findings revealed the following: Hb 13 Gm, R B C 4.3 million, W B C 6,000, with a normal differential count, platelets 66,000, urine free from bile. Kline Negative. Prothrombin time (Orrich) 30.8 seconds, capillary and red blood cell positively normal. Bromsulphalein test 60 per cent retention in 30 minutes, cephalin flocculation test 3 plus, phosphatase 6, serum protein 7.5 Gm, albumin 3.5 Gm, (A/G ratio reversed) globulin 4.0 Gm, bilirubin 1.5 mg. Chest film normal. Plain film. Enlarged spleen. Complete cystoscopy, with retrograde pyelograms, showed no abnormality. A roentgenogram of the esophagus showed early varices.

Course The patient was treated with a high vitamin, high carbohydrate, high protein, low fat diet, supplemented with Brewer's yeast, liver and betabione. On the 27th hospital day the patient was operated upon and a moderate amount of ascitic fluid was present. Following the removal of the spleen (weight 620 Gm) and left kidney, an

anastomosis between the left renal vein and splenic vein was carried out, using an 8-Mm vitallium tube. The pressure in the coronary vein before the anastomosis was completed was 400 Mm of water, and following the completion of the anastomosis the pressure measured 240 Mm of water. A biopsy of the liver revealed Laennec's cirrhosis of the liver with a moderate degree of healthy-looking hepatic cells in the areas of regeneration. The postoperative course was complicated by a mild bronchopneumonia, and it was necessary to perform several paracenteses. He was discharged, on the 21st postoperative day.

Follow-up Six weeks following operation the patient's only complaint is some itching of the skin. He has a good appetite. Has gained weight and strength. On examination, he appears much improved. His color is good. There is no evidence of ascites. Laboratory findings: Serum total proteins 6.7 per cent, S G 4 S A 2.7 N P N 33 mg per cent. Serum bilirubin 2.1 mg per cent. Cholesterol 251 mg per cent. Inorganic phosphatase 3.5 mg per cent. Alkaline phosphatase 8.9 Brodsky units. Hippuric acid excretion after one hour = 0.5 Gm. Cephalin flocculation test = \pm .

COMMENT—Whereas, there have not been a sufficient number of cases operated upon, nor has there been sufficient time elapsed since operation to judge the efficacy of this procedure, the results, so far, appear to warrant further trial.

The recurrence of an episode of bleeding in the child with cirrhosis (Case 5) 14 months after operation does not, in our opinion, necessarily mean that the portal-caval shunt has become blocked. It may mean, due to the effects of nitrogen retention upon blood pressure, *etc.*, that the combined blood-carrying capacity of the shunt and the collateral vessels were overtaxed for the time.

SUMMARY

A nonsuture method of blood vessel anastomosis, using vitallium tubes, is presented. Cases are reported to illustrate its use in acute traumatic vascular injuries, traumatic arteriovenous fistulae, peripheral arterial aneurysms, and the establishment of portal-caval shunts for the relief of portal hypertension.

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DISCUSSION—DR ALFRED BIALOCK, Baltimore, Md Last year at the meeting of this Association I took the liberty of speaking about Doctor Blakemore's method for wiring aneurysms and of the excellent results which he has obtained I am sure that this method has not received the amount of attention it deserves I am delighted that Doctor Blakemore is here in person this year and that he has presented work on the use of a nonsuture method for bridging gaps in blood vessels

I would like to describe briefly the result which followed the use of the vitallium tube in connecting the splenic vein and the renal vein in a patient with cirrhosis of the liver This patient, age 47, became ill 18 months ago It was noted that the abdomen had increased in size She entered Johns Hopkins Hospital in February of this year, and it was necessary to tap the abdomen frequently, approximately six liters of fluid being removed each week There was a temperature elevation each day to approximately 102° F, and the patient's condition was considered very poor About a month following entrance to the hospital a left transverse abdominal incision was made and the spleen and left kidney were removed The spleen showed scarring and congestion and a section of the liver showed advanced cirrhosis The splenic vein was then anastomosed to the left renal vein by the use of a vitallium tube The patient's postoperative course was fairly uneventful Fluid accumulation within the abdominal cavity continued for a while, but at a somewhat reduced rate The fluid accumulation apparently stopped during June, and she has not had to be tapped for almost six months (slide) This slide shows the vitallium tube in place, and this slide is a recent photograph of the patient, there is no evidence of ascites

The nonsuture method for connecting blood vessels is of great value when the ends of vessels cannot be approximated without tension I do not think that the nonsuture method has particular merit in the case of anastomosis of the splenic and renal veins Anatomically, these structures lie very close to each other and I think it is probably better to anastomose the veins directly, end-to-end, without the use of tubes As a matter of fact, we performed such an anastomosis several weeks ago and no unusual difficulties were encountered These remarks are in no way meant to detract from the value of the method which has been devised by Doctors Blakemore, Lord, and others

As I have indicated, and as is generally known, it is not always necessary to use a tube in anastomosing blood vessels Doctor Faussig and I have been working on the hypothesis that an artificial patent ductus would be helpful in the treatment of pulmonary stenosis Approximately a week ago we anastomosed the proximal end of the divided left subclavian artery to the side of the left pulmonary artery This was done by arterial suture The time since operation has been too short to know whether this 15-months-old child will be improved When one can anastomose vessels by the suture method without undue tension, it seems to me that the procedure is preferable to the use of a large foreign body This statement is made with full realization that there are many instances in which part of the length of vessels is destroyed, in which a tube must be used if the continuity of the vessel is to be restored It is in such instances as these that the Blakemore method would result in the saving of structures which would otherwise be lost

DR. RUDOLPH MATAS, New Orleans, La I cannot resist the tempting opportunity to join in the discussion of Doctor Blakemore's paper, as I have been deeply interested in the success of his experimental studies ever since their publication When I first learned the details of his technic, I looked upon his sutureless method of uniting divided arteries as the culminating point in the long history of arterial reconstruction and repair, and the solution of a problem which for nearly two centuries has exercised the ingenuity of surgeons The ideal of surgery in dealing with injuries of the great arteries has been, always, to restore the continuity of the circulation directly through its main channels independently of the secondary or collateral branches The innumerable methods which have been devised to unite divided arteries suffices to show the importance attached to this principle and the difficulties that have been in the way of its performance

The great merit of Blakemore's work is that in his efforts to simplify and perfect his sutureless method of repairing and rehabilitating wounded arteries, he has devised

a technic which utilizes all that is best in the experience of his predecessors while availing himself of contemporary discoveries in hemo- and chemotherapy which have profoundly modified and improved the treatment of war wounds. In this way he has created a new type of vascular anastomosis which is the embodiment or synthesis of all that is best in the old and in the new of vascular surgery. By dispensing with the delicate and time-consuming methods of suture, and by utilizing preserved heterogenous venous grafts, already mounted on vitallium tubes, he has reduced the time limit of anastomosis to its minimum terms. Besides these technical innovations, he has reinforced his defences against infection by resorting to the sulfas and penicillin, and against thrombosis, by the systematic use of heparin. In this way he has accomplished the great objective of his endeavors by making the rehabilitation of damaged arteries practicable at the battle fronts, in the field hospitals where vascular rehabilitation is most indicated. In this respect he has improved on the practice of the German surgeons in World War I, who anastomosed the arteries by suture on the Carrel principle (with and without venous grafts) and made this the method of election in dealing with the main arteries, only resorting to the ligature for minor vessels. These operations were performed chiefly at base hospitals for pulsating hematomas and traumatic aneurysms which could wait for deliberate treatment.

Their statistics show that, despite a considerable number of failures by thrombotic occlusion and other causes, the results in the saving of limbs from amputation were, in general, decidedly better than those obtained by the permanent ligation of the vessels involved, with sole dependence on the collateral circulation.

It is evident that Doctor Blakemore, by applying his simplified and quick method of anastomosis, has made this procedure as available in the field as in the rear hospitals and, in so doing, has added a most valuable and timely contribution to vascular surgery in general and to war surgery in particular. And this is important in view of the great increase in the number of wounds of the lower extremities caused by ground mines and fragmentation of explosive shells and bombs, *etc.*, which are so extensive and destructive to the soft parts that they not only damage the main arteries but a large area of the regional collaterals, with consequent increase in the amputations of the lower extremities.

In going over Doctor Blakemore's publications I have been impressed by the earnestness and scientific ability with which he, and his associates, have pursued their experimental work and the ingenuity with which they have overcome obstacles which have blocked the way of their predecessors (*e g.*, preserving, preparing and utilizing heterogenous venous grafts on a large scale—a sort of bank of venous grafts).

It is noteworthy that Doctor Blakemore has not minimized the importance of the collaterals, despite his special plea for the major circulation. In fact, he is concerned in the best means of prolonging their functional efficiency. His classifications of war wounds according to the extent and degree of the damage done to the circulation shows that he is not indiscriminate in the selection of the cases in which his reparative anastomosis is really indicated.

After reviewing the experimental and clinical evidence of the practical efficiency of the "sutureless anastomosis" so convincingly presented in Doctor Blakemore's publications, it would seem that nothing remains but to test his procedure at the battle front, in the special type of casualties which this monstrous war so abundantly and unfortunately provides.

In the meantime, Doctor Blakemore, and associates, are entitled to congratulations and praise for an achievement which marks the most notable advance in the contemporary surgery of the peripheral blood vessels.

DR ARTHUR H. BLAKEMORE, New York, N. Y. (closing) Doctor Blalock has presented two cases of cirrhosis of the liver in which he performed splenic-venal vein anastomosis for the relief of portal hypertension. He demonstrated, in the second case, his complete mastery of blood vessel suture technic in choosing to perform a suture anastomosis. This was a surgical feat deserving of the highest congratulations.

I want to express my appreciation to Doctor Matas for his most generous remarks. I welcome this opportunity to thank Doctor Matas in behalf of my associates and myself for the many wise and helpful suggestions he has given us in the development of this work.

END-RESULTS IN THE TREATMENT OF HYPERPARATHYROIDISM*

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THE EARLY THIRTIES were the golden years of progress in the surgery of the parathyroids in this country. Pioneer work was done by Ballin and Morse,¹ of Detroit, but the Boston group easily outstripped all the other clinics by finding and operating upon 78 cases in 12 years^{2, 3, 4}. Since Cope, of that group, maintains that this large series was attained without a great number of referrals from a distance, it seems almost necessary to postulate a geographic factor. During the same period, only 15 cases of hyperparathyroidism, proved at operation, were encountered at the Mayo Clinic,⁵ and only six cases have been recognized at the Henry Ford Hospital. Undoubtedly, both of these clinics were well enough aware of at least the skeletal manifestations of the disease at an early date because Pemberton's⁶ successful removal of a parathyroid adenoma antedated the operation on Case 1 of the Boston series by more than a year and, in 1931, one of us (R D McC) searched for an adenoma in the neck of a patient with marked osteoporosis. The pathologist could find no parathyroid tissue in the excised specimens, and in the light of fuller knowledge of calcium metabolism, this particular case cannot be classified as one of hyperparathyroidism, but it may be worth while to record that following exploration and partial thyroidectomy, the patient ceased to have bone and muscle pain for which he had sought relief. He died four years later of carcinoma of the sigmoid.

No attempt will be made to give a complete account of all the symptoms and signs which may be encountered in disease of the parathyroid glands. The history of urinary calculi, skeletal abnormalities, particularly pathologic fractures, bone and muscle pains and even such general symptoms as lassitude and constipation should arouse suspicion. Roentgenograms of the skull and long bones give confirmatory evidence. Laboratory tests clinch the diagnosis. Typically, there is elevation of the serum calcium and phosphatase, and lowering of the serum phosphorus. There is a negative calcium balance as a result of the increased urinary excretion. The urine test described by Sulkowitch gives a rough estimation of this calcium loss.⁷

In our small series of six cases may be found examples of all of the clinical types of hyperparathyroidism, classic von Recklinghausen's disease, osteoporosis with and without renal stones, renal stones alone and a type which has been called acute parathyroid poisoning. It is to the credit of the Boston group that their series included no instance of the latter type, which is associated with the implication that specific surgical treatment was withheld or delayed until there was a fatal issue. Such was the unfortunate

* Read before the Fifty-sixth Annual Session, Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

result in Case 1 of our series, which is included even though the patient was never seen by a general surgical consultant

CASE REPORTS

Case 1—K E (169909) was a white woman, age 44. She was admitted to the Henry Ford Hospital, November 3, 1931, with the complaint of pain in the right chest and right thigh. Four months before, she had sneezed violently and felt a tearing sensation in the right side. Pain persisted and two months later there was also discomfort in the right thigh. Just previous to admission, the symptoms of dyspnea,



FIG 1—Case 3, shortly after operation. Note the extreme emaciation.

weakness and anorexia appeared. The chief finding on physical examination was dullness at the right lung base, which was correctly interpreted as fluid. Three hundred cubic centimeters of serosanguineous fluid was removed by thoracentesis. An examiner reported that this fluid contained "many blood cells and a few large cells with abundant cytoplasm and hyperchromatic nuclei suggestive of a malignant process."

Roentgenograms of the right femur showed "A destructive process involving the lower one-third of the bone. There are several areas of decreased density seen in the anteroposterior position which would appear to be separated from each other by more or less normal bone. The picture suggests metastatic malignancy."

These two "suggestive" findings were so convincing that an excellent internist then stated "Further investigation is of academic interest only. She is financially unable to have more studies, and from the practical standpoint, it makes no difference since in any event the outlook is hopeless. She should be kept in bed to prevent a pathologic fracture." Deep therapy was administered to the femur and she was discharged on December 2, 1931. She was readmitted on December 26, 1931, on account of inability to eat and vomiting. In four days of symptomatic treatment, she felt well enough to go home. As she stepped into a waiting automobile, the left leg collapsed. She was carried back to her room, and roentgenograms showed a pathologic fracture of the lower third of the femur, for which skin traction was applied.



FIG 2

FIG 2—A Skull before operation, Case 3
B Skull eight years later, normal appearance

Dr Carl Badgley saw the patient on December 31, 1931, and stated "The development of pathologic fracture in the left leg, with roentgenologic evidence of cystic degeneration with similar lesions developing elsewhere in the skeletal framework, makes the possibility of a parathyroid lesion resulting in an osteitis fibrosa cystica presumptive. We would like to know how authoritative the report of the malignant cells in the pleural fluid is. Calcium and phosphorus studies are advised. Also, it is suggested that Doctor McClure see the patient in consultation with regard to the advisability of parathyroid surgery." On this day the serum calcium was 14.3 mg and the phosphorus was 2.57 mg.

January 8, 1932. Continues to be nauseated and vomits nearly every day.

January 13. Serum calcium, 19.4 mg, phosphorus 3.88 mg.

January 20. Hemoglobin 9.2 Gm. Mental status very cloudy.

January 25. Carbon dioxide combining power, 68.5 vols per cent (alkalosis from vomiting).

February 13. Temperature higher. Patient very pale, with a waxen appearance. Serum calcium, 14.2 mg, phosphorus 6.25 mg.

February 14. Patient weaker, unable to drink through tube. Temperature 103° F.

February 15. Patient expired.

Autopsy. It was found that the parathyroid glands were diffusely enlarged, and the microscopic picture was that of hyperplasia. There were calcium deposits in the lungs, kidneys and blood vessels. The cystic areas in the bones showed the usual picture of advanced osteitis fibrosa cystica.



FIG 3—A Femur, Case 3, before operation, shows lacunar osteoporosis.
B Femur, eight years after parathyroid tumor was removed.

This case is very similar to that reported by Hanes.⁸ Dr Fuller Albright wrote Dr Hanes "It is my belief that your patient died of parathyroid poisoning which is a complication of hyperparathyroidism, which occurs when the blood calcium rises above a certain critical point. At this critical point the serum phosphorus, instead of being low, starts going up because phosphorus is no longer diffusible at very high levels of calcium. The thing which would have alarmed me about your case was not so much the high calcium as the absence of low phosphorus." Surgery was not carried out on Hanes' case on account of the unexplained fever. In our case, the record fails to disclose why the suggestion of a general surgical consultation was not followed through.

Case 2—Already reported in the surgical literature.⁹ E. D., (196988), female, age 51, showed the lesions of typical osteitis fibrosa cystica and a pathologic fracture of a femur. In March, 1934, a cystic parathyroid adenoma imbedded in the lower part of the right thyroid lobe was removed. There was immediate symptomatic improvement, but

the patient expired four months later in an hypoparathyroid state. It must be presumed that the blood supply to the remaining normal parathyroid glands was disturbed by the operative procedure.

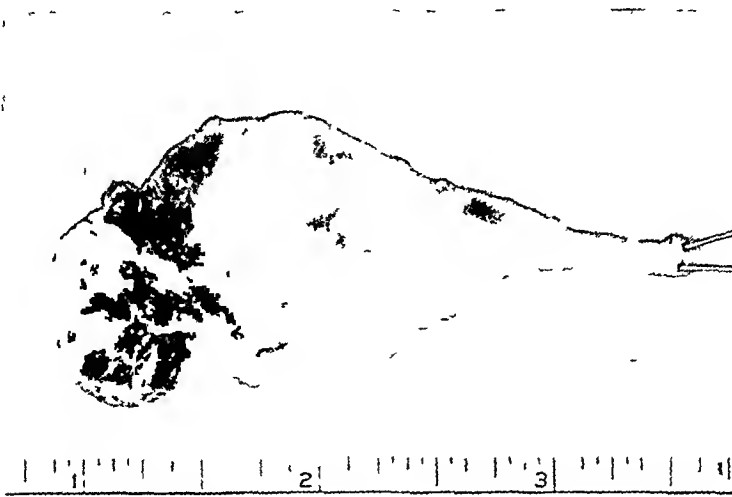


FIG. 4—Parathyroid adenoma removed from Case 3

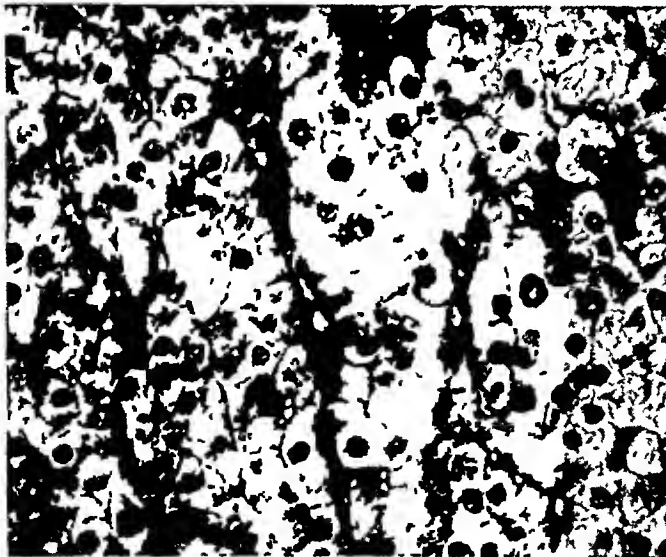


FIG. 5—Photomicrograph of tumor from Case 3. It is composed of oxyphilic cells.

It is more of a pleasure to report on the follow-up of the remaining four cases in our series.

Case 3—J. H., (229176), a toolmaker, age 51, was admitted on January 18, 1936, complaining of "rheumatism" of seven years duration. Over this period, stiffness and pain which began in the feet gradually involved the knees, shoulders and elbows. Marked muscular weakness appeared and this progressed to the point where walking was difficult. Constipation was troublesome. There was a weight loss of 30 pounds. The patient

presented a picture of cachexia (Fig 1) There was little or no subcutaneous tissue, the flaring costal margins accentuated the scaphoid appearance of the abdomen Generalized bone tenderness was present The dorsal spine was kyphotic Urinalysis was normal Wassermann negative The blood count indicated secondary anemia, with 3,400,000 red blood cells and 45 per cent hemoglobin

The marked emaciation, anemia and constipation suggested the provisional diagnosis of gastro-intestinal malignancy However, Dr F J Sladen noted that the past history contained a note of three attacks of urinary stone passage and suggested studies of parathyroid function Roentgenograms of the skull showed the typical granular appearance (Fig 2 A) and the long bones showed osteoporosis of the lacunar type (Fig 3 A) There was marked demineralization of the spine Small areas of calcification were seen throughout both kidney area The diagnosis of hyperparathyroidism as confirmed by the finding of a serum calcium of 19.3 mg, serum phosphorus of 3.53 mg, and phosphatase of 7.13 Bodansky units Careful examination of the neck revealed the probable existence of a nodule in the region of the right lobe of the thyroid gland

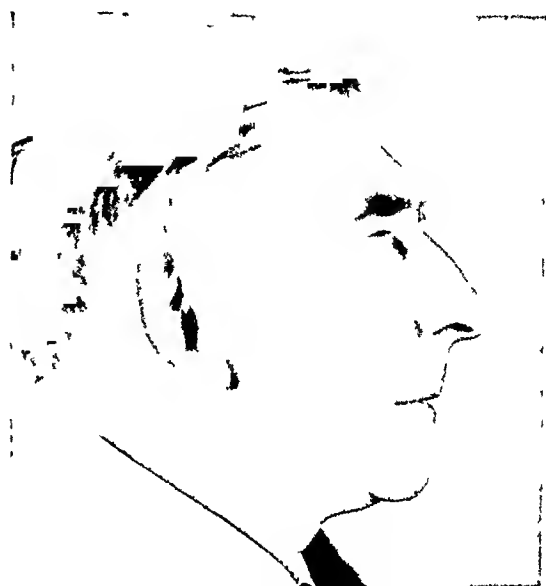


FIG 6—Case 3, eight years after operation

Operation—February 5, 1936 The usual thyroid exposure was affected A plum-sized tumor lay behind the right lobe of the thyroid, displacing it forward It could be lifted out of its bed easily, since

the vascular attachments were long The tumor weighed 13 Gm, and measured $3 \times 2.5 \times 1.7$ cm (Fig 4) Microscopic examination of the tumor revealed it to be an adenoma composed chiefly of oxyphil cells (Fig 5)

The day following operation, the patient stated that he felt better than he had in months On the second postoperative day, the serum calcium was 9 mg and five days later it was 7.8 mg He was given a high calcium diet and cod liver oil On March 2, an inguinal hernia was repaired and he was discharged shortly thereafter He returned to work in May By November, he had gained 44 pounds The recalcification of the bones was watched by frequent roentgenograms Two years after operation, there was little abnormal Recent pictures of the skull and a femur show normal bone architecture (Figs 2 B and 3 B) Slight calcification in the kidney areas has persisted and the patient recently consulted the Urology Department about mild urinary symptoms The phenolsulphonphthalein test showed normal kidney function His general health is excellent, and he works regularly as a toolmaker in a war plant (Fig 6)

Case 4—C B, (50822), white, male, age 19, was seen in consultation by the senior author at the Charles Godwin Jennings Hospital in January, 1938 The patient had been troubled with renal calculi since August 1, 1937 Early roentgenograms (Fig 7) had shown a number of stones on the right side and one on the left Several cystoscopic procedures were carried out by Dr G E Chittenden during the next four months There was marked increase in the size of the stones in the right kidney (Fig 8), and on January 12, 1938, Doctor Chittenden removed some of the stones by pyelotomy and left in a nephrostomy tube Progress roentgenograms showed many stones remaining On January 26, the serum calcium was 15.8 mg Dr Robert C Moehlig saw the boy in consultation and advised exploration of the neck for parathyroid tumor A radiograph of a femur showed little deviation from the normal

Operation—February 1, 1938 The vicinity of the right lobe of the thyroid was explored first and no definite parathyroid tumor could be found. At the tip of the lower pole, attached to the thyroid gland, was a small round body about one centimeter in diameter, with the brownish-red color of thyroid tissue. The left lobe was then examined and nothing unusual was found in contact with any part of it. About one centimeter below and lateral to the lower pole, there could easily be seen a definite, smooth,



FIG 7—Roentgenograms of kidney areas on October 15, 1937 Case 4

encapsulated oval structure, about $2 \times 1.5 \times 1$ cm in dimensions, of about the same consistency as normal thyroid tissue and for the most part, of a brownish-red color. The structure was loosely attached to the base and sides of the left thyroid fossa by delicate blood vessels and areolar tissue. This was thought to be the parathyroid tumor, and it was excised. The nodule attached to the lower pole of the right lobe of the thyroid was also removed. The pathologist, Dr F W Hartman, reported that the ovoid tumor from the left side was a parathyroid adenoma composed mainly of chief cells, while the nodule from the right was thyroid tissue (Fig 9).

His convalescence was uneventful. Roentgenograms ten days later showed a diminution in the size of the calculi in the right kidney. On February 14, the serum calcium

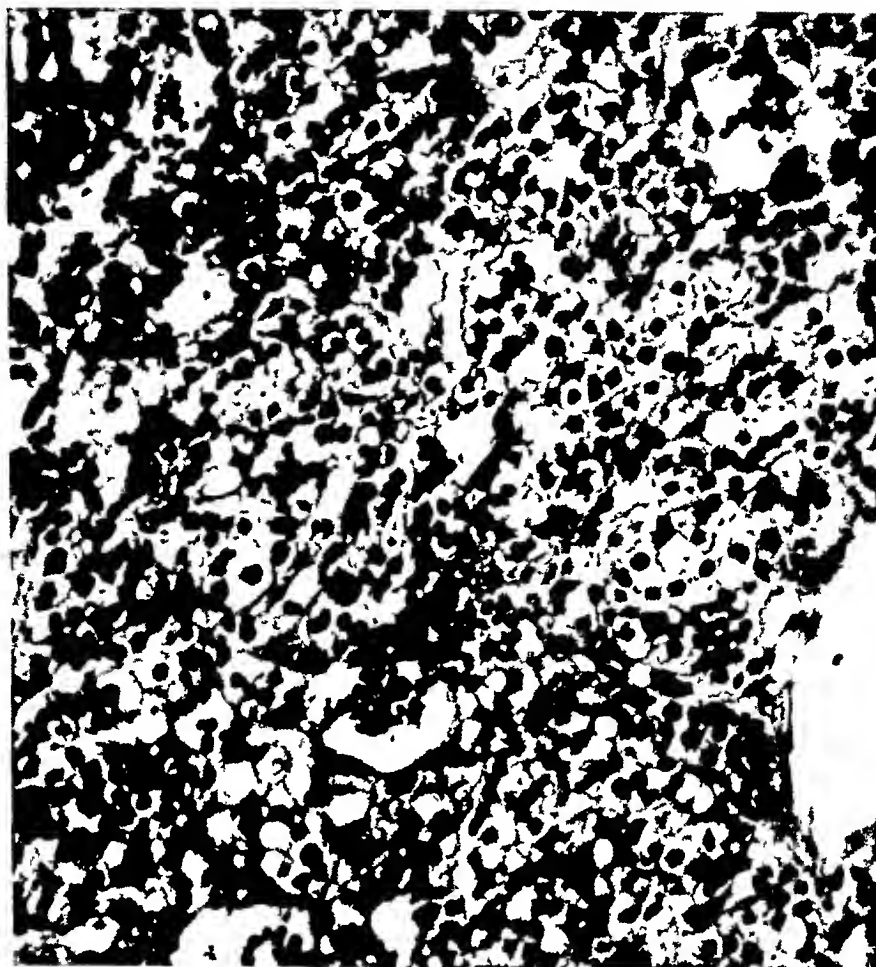


FIG 9 —Photomicrograph of parathyroid tumor removed from Case 4



FIG 8 —Plain film of right kidney area, January 12, 1938 Case 4
There has been an increase in the size of the stones

was 10.9 mg. Roentgenograms taken on August 2, 1938, showed no sign of calcification about the kidneys (Fig 10). Six years later, in August, 1944, there were no urinary symptoms and no roentgenographic evidence of stones.

Case 5—R. K., (287639), white, female, age 14, was admitted on the orthopedic service, February 6, 1939, complaining of "knock-knees." The legs had been straight a year before, but there had been rapid development of the genu valgum deformity.



FIG 10—Roentgenograms of kidney areas on August 2, 1938, Case 4, showing disappearance of all kidney stones.

(Fig 11 A) For several months, she had been taking extra calcium and vitamin D on the advice of her physician. The serum calcium averaged 15.3, the phosphorus 2.61, and phosphatase 6.37 Bodansky units. A calcium balance study showed a calcium excretion of six times normal. Roentgenograms of the knees showed the marked genu valgum deformity with persistence of the epiphyseal lines. Osteoporosis, with coarse trabeculation, was seen in the long bones and the skull showed a granular type of osteoporosis.

Operation—March 4, 1939. The region of the right lobe of the thyroid was explored first, and no tumor was found. On the left, below and lateral to the lower pole, there was a bean-shaped body, measuring 2 x 1 x 1 cm, darker red in color than thyroid.

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tissue (Fig 12) The tumor was found to be an adenoma composed of chief cells (Fig 13) On the second postoperative day, the patient had a positive Chovstek sign and some numbness and tingling of the fingers Calcium and viosterol medication was started immediately and the signs of impending tetany disappeared within a few hours Convalescence was otherwise uneventful Three weeks after the operation, the serum calcium was 10.2 mg, phosphorus 3.04, and phosphatase 4.39 units

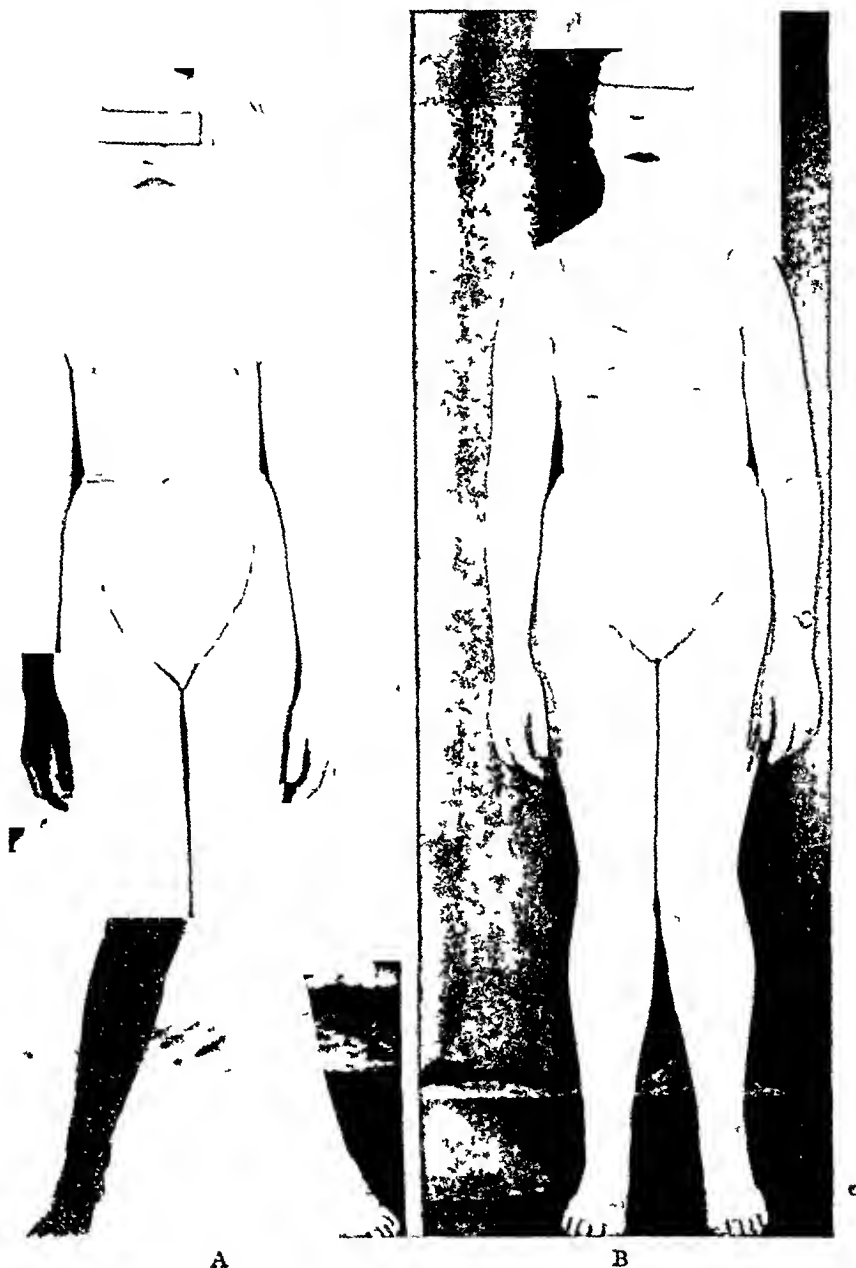


FIG 11—Case 5 A Preoperative photograph, March, 1939
B Postoperative photograph, October, 1944

It was presumed that an osteotomy would be necessary for the correction of the deformity of the knees However, when the patient was seen for follow-up, November 11, 1939, the malleoli were already three inches closer She stated that she was less nervous and did not tire as easily She was not seen for five years Follow-up letters were not answered, possibly because the patient and her father feared that the operation would be insisted upon However, in October, 1944, she deemed it safe to return A gratifying correction of the genu valgum had taken place (Fig 11 B) Serum calcium, phosphorus and phosphatase were normal

Case 6—C S, (311593), female, age 18, was admitted to the hospital, May 19, 1940, complaining of a lump in the neck and pain in the right hip. Inspection of the neck revealed an obvious nodule in the region of the right lobe of the thyroid (Fig 14)



FIG 12—Photograph at operation (Case 5) showing parathyroid adenoma *in situ*, where it lay behind the lower pole of the left lobe of the thyroid

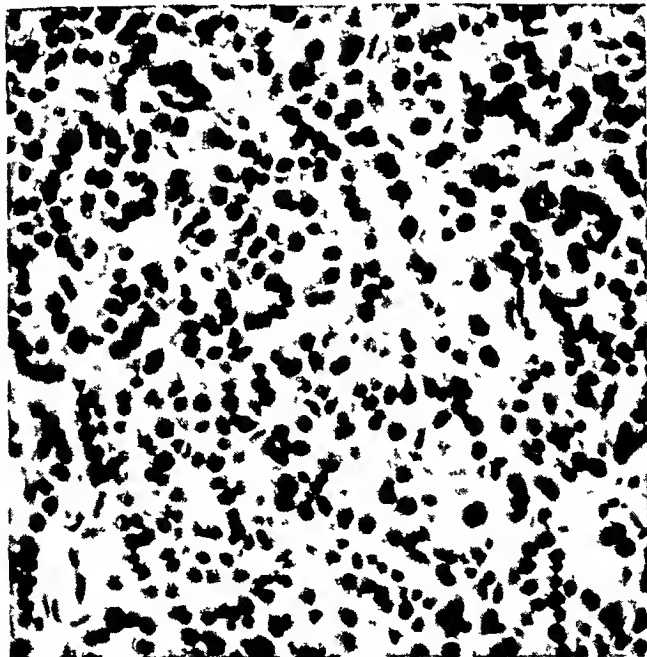


FIG 13—Photomicrograph of adenoma (Case 5)

Roentgenograms showed typical osteitis fibrosa cystica. On May 24, the serum calcium was 16.5 mg, phosphorus 2.9 mg, phosphatase 13 Bodansky units.

Operation—May 28, 1940. No tumor could be found on the left side. On the right,



FIG 14—Case 6, showing visible nodule in the neck

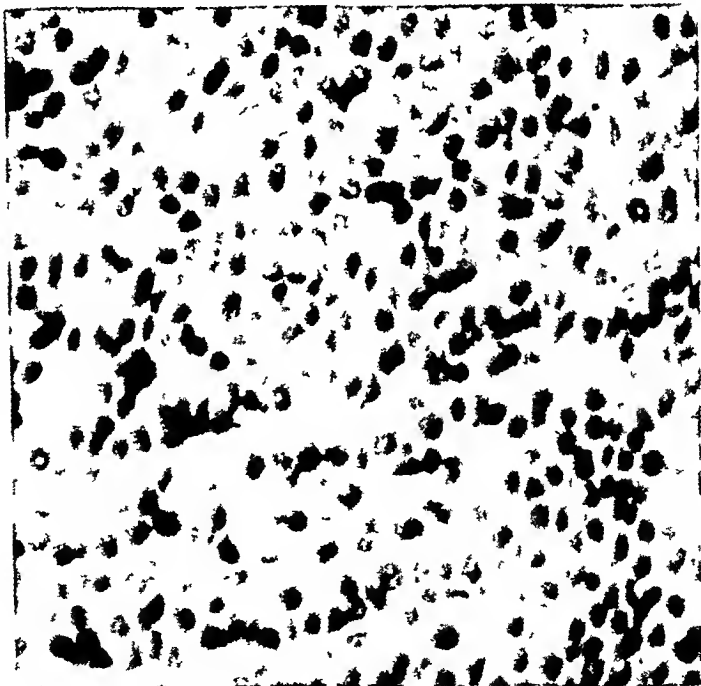


FIG 15—Photomicrograph of adenoma removed from Case 6

there was a definite tumor which felt as though it were behind the thyroid gland, pressing up into it. The entire right lobe of the thyroid including this nodule was removed. The tumor proved to be a parathyroid adenoma of the chief cell type (Fig 15).

Two days after the operation, the serum calcium was 6.9 mg, the phosphorus 3.22, and the phosphatase 3.2. She was given large doses of calcium and vitamin D. There was an increase in the serum calcium, and she was discharged on June 8. However, it was necessary to hospitalize her again on June 10 on account of the appearance of numbness and tingling of the fingers suggestive of impending tetany. After a week of calcium therapy, she was discharged. Follow-up in December, 1944, showed the patient to be asymptomatic. Progress roentgenograms revealed considerable recalcification of the bones. Serum calcium (not fasting) was 11 mg.

SUMMARY

Six cases of hyperparathyroidism have been reported. One patient did not have surgical intervention, and expired with the picture of acute parathyroid intoxication. Adenomata were removed from the other five patients. One of these died four months after operation in an hypoparathyroid state. The remaining four patients have been followed from eight to four years after operation, and appear to be normal individuals.

It is hoped that the report of this small series will serve as a reminder of the existence of the disease of hyperparathyroidism, and that it will encourage further reports of late results.

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DISCUSSION—DR FRANK H. LAHEY, Boston, Mass. I think it is a very nice thing to have the subject of hyperparathyroidism brought up occasionally because I am sure that a great many parathyroid adenomas are being overlooked constantly.

I would always like to pay tribute to the group at the Massachusetts General Hospital, in Boston, who have done such fine work on parathyroids, and particularly to Doctor Fuller Albright.

I would particularly like to call attention to the danger of tetany in these patients with hyperparathyroidism who have had parathyroid adenomas removed. In the slides will be shown a large parathyroid adenoma (Fig 1) removed from a patient with hyperparathyroidism about two weeks ago, and the calcium estimations morning and night.

immediately after operation (Fig 2) It is of interest to note how rapidly the blood calcium can drop in 48 hours to half the point at which it was before operation We must all realize that many of these patients with hyperparathyroidism, unless they are watched carefully, will go into tetany and will unnecessarily go through the emotional ordeal of this frightening episode We must all realize that the overactive parathyroid adenoma largely takes over the function of the other parathyroid glands and so these patients require a few weeks before their remaining parathyroids resume their activities after the toxic adenoma has been removed We have been extremely careful to protect these patients from tetany, who have had parathyroid adenomas removed, with administrations of calcium and A T-10 and to withdraw this medication gradually so that more and more load can be thrown upon the remaining parathyroid glands, and so that they will gradually resume their activities

We have learned a good deal in our search for parathyroid adenomas about the locations where they can be found One should never fail to release the upper pole of the thyroid by tying the superior thyroid artery and vein and pulling the upper portion of the thyroid away from the larynx because the upper parathyroid is so frequently behind the upper pole, and gets molded into the gland We have reported three intra-thyroid parathyroids found at this point

Another thing which is of great assistance is to expose the inferior thyroid artery carefully and dissect it in a dry field from well down behind the common carotid up to its entrance into the gland, carefully preserving each branch If a branch is found coming off the trunk and running toward the mediastinum, and this branch is followed down, it will often lead to a mediastinal adenoma or an adenoma in the areolar tissue beneath the clavicle

I am sure we need to do more frequent blood calcium determinations in people with nerve root pressure symptoms, with muscle pains, with kidney calcification and renal stones, in order that we can discover parathyroid adenomas before these patients have reached the stage of osteitis fibrosa cystica or before spontaneous fractures have developed

DR HUGH A GAMBLE, Greenville, Miss I want to emphasize the remarks of Doctor Lahey, that the disease is not as rare as we think I am from a rural district and a small community, and I have seen two cases of this condition diagnosed preoperatively, with recovery in both cases

There is another phase of the subject I would like to emphasize I believe that the parathyroids have more to do with calcium metabolism than any other organs We see a great many cases of postmenopausal osteoporosis of the spine in which there is decalcification of the spine and the spinal vertebrae become crushed These patients suffer a great deal Personally, I believe the parathyroids have much to do with this decalcification, and while the blood picture is not usually changed as much as we find in adenoma of the parathyroids, the blood calcium is usually elevated above normal and the phosphorus is lower than the average

In three of these cases I have at operation demonstrated the parathyroids and removed half of them Two patients were relieved entirely symptomatically and the progress of the disease was stopped The third patient obtained no relief I think, however, that a further study relative to the influence of the parathyroids upon postmenopausal osteoporosis of the spine is well worth emphasizing

A few years ago Albright brought out a report of 42 cases of this condition in which he claimed that the pathologic changes present were always due to postmenopausal conditions He reported only one case in this series of adenoma of the parathyroids However, I am firmly convinced that the absorption of calcium in this condition is more influenced by the action of the parathyroids than in any other way, and I feel that these patients should be studied more carefully and our results in their treatment would no doubt be improved

DR THOMAS D SPARROW, Charlotte, N C Doctor McClure and Doctor Lam have given us a most interesting and instructive discussion of the end-results of the treatment of hyperparathyroidism Perhaps the remarks that I am about to make are not germane to this discussion, however, it does concern the activity of the parathyroid gland and the result obtained in its removal

Many authors have questioned whether or not the parathyroids are an etiologic factor in calcinosis universalis. Since in this condition there is a definite disturbance of the calcium metabolism, the finger of suspicion is at least pointed to the parathyroid glands. The fact that as a rule the blood calcium and phosphatase are normal in calcinosis universalis, would lead to the opinion that there is no active hyperparathyroidism in this disease.

Ramsdell has removed the parathyroid in several cases and has reported improvement of the condition. He suggests that this may be due to a dysfunction of the parathyroid rather than to an hyperparathyroidism.

My reason for entering this discussion is that recently we have had the opportunity of observing a case of calcinosis universalis in which the parathyroids were removed and in which there was a high blood calcium and a high phosphatase. I would like briefly to report the results obtained in this case.

On September 9, 1943, a boy, age 12, was admitted to the Orthopedic Service of the Charlotte Memorial Hospital, complaining of a swollen, tender right knee, and numerous nontender masses on both thighs, about the knees, elbows and in the axilla. These masses had been present for three months. The right knee had been very tender and painful for about one week. Three years prior to this admission, the patient had complained of severe pain in his back, and had become very weak and cachectic, with a considerable amount of muscular atrophy. There were numerous small, firm, ovoid and round masses palpable in the subcutaneous tissue about the elbow joints and in the axilla. Both thighs were swollen and fluctuation could be elicited above the knee. The right knee was very tender and painful. His temperature rose to 104° F the next day. He was given sulfadiazine, and hot applications were applied to the painful right knee and thigh. On the ninth hospital day the right knee was aspirated and pus was obtained, it was incised and drained three days later. Thereafter, the temperature remained normal. On the 15th hospital day the left thigh was aspirated and about 400 cc of a thick, white, milky-looking fluid was obtained which, on analysis, showed calcium 3.7 mg per 100 cc, protein 7.8 mg per 100 cc, and cholesterol 200 mg per 100 cc.

A pathologic study of a biopsy on one of the masses near the elbow showed it to be a calcium granuloma. The roentgenologic examination led to the diagnosis of calcinosis universalis. This diagnosis was questioned when it was known that there was a high blood calcium and a high phosphatase present. The tests were checked and rechecked and run against normal controls, and proved to be correct readings. Because of the high blood calcium and high blood phosphates it was decided to perform a parathyroidectomy.

Under general anesthesia, two parathyroid bodies were identified and removed. Histologic examination proved the tissue to be parathyroid bodies.

The laboratory findings were as follows:

Date	Calcium	Phosphorus	Phosphatase	Sulkowitch Test
9-13-43	17.6 mg %	4.3 mg %	9.8 units	
9-15-43				Markedly positive
9-17-43	16.9 mg %	4.1 mg %	9.0 units	Markedly positive
9-27-43	16.2 mg %	4.1 mg %		
10-11-43	15.1 mg %	4.0 mg %	9.6 units	Markedly positive
REMOVAL OF PARATHYROID GLANDS				
10-20-43	14.8 mg %	4.0 mg %	9.1 units	
10-26-43	15.0 mg %	4.4 mg %	8.3 units	
11-27-43	12.7 mg %	4.0 mg %	6.6 units	Negative
1-3-44	13.0 mg %	4.2 mg %	5.0 units	Negative
2-21-44	14.2 mg %	3.8 mg %	5.0 units	Negative
4-10-44	11.7 mg %	3.8 mg %	4.5 units	Negative
8-10-44	10.8 mg %	3.3 mg %	3.8 units	Negative
10-9-44	16.0 mg %	4.0 mg %	2.1 units	Negative

1 This case is reported as a case of calcinosis universalis in which there was a high blood calcium and high phosphatase.

2 The removal of the parathyroids resulted in a marked clinical improvement and lowering of the phosphatase (Bodansky units).

HYPERPARATHYROIDISM

3 Parathyroidectomy resulted in reducing of the calcium excretion in the urine Whether or not it had any effect on the blood calcium is questionable

DR JOHN DEJ PEMBERTON, Rochester, Minn I want to say a word regarding the incidence of this disease, and express my conviction that it is much higher than is generally supposed Doctor Lam spoke of our series of 15 cases which we had observed up to few years ago About two years ago, one of my colleagues, Doctor Keating, spent six months in Boston at the Massachusetts General Hospital with Doctor Albright and his associates, and since his return we have seen as many cases of hyperparathyroidism in the Mayo Clinic as we saw in the ten preceding years

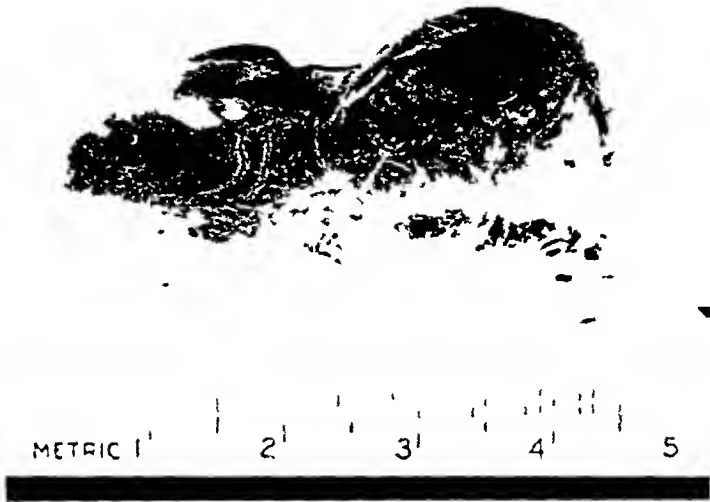


FIG 1

DR ROY D McCLURE, Detroit, Mich (closing) We were keenly disappointed in the end-result of our second case This was the patient who expired four months after operation, with the typical signs of parathyroid insufficiency The difficulties of dealing with such a situation, and the feeling of helplessness which one has, cannot be stressed too strongly The case was discussed with Doctor Churchill and it was agreed that it is advisable to carry out partial resection of certain of the larger adenomas followed by a second stage if necessary

More frequent diagnoses of the condition may be expected when doctors are well informed of the signs and symptoms and are on the lookout for them Urologists, in particular, are in an excellent position to spot the cases

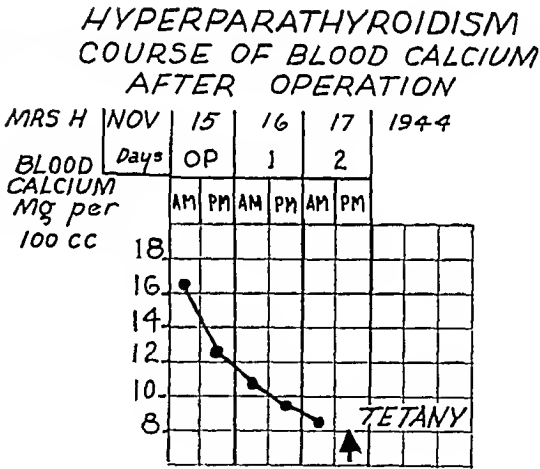


FIG 2

CASES OF SEVERE PELVIC INJURY*

LT COL LLOYD G LEWIS, M C

WASHINGTON, D C

PELVIC INJURIES are frequently complicated by wounds of the urethra, bladder and ureters, which require immediate diagnosis and prompt surgical treatment

Diagnosis must be made by evaluation of clinical signs. Symptoms lack specific reference. Systematic observation for wounds of entrance and exit, ecchymosis, swelling, palpation of tissues for extravasation of blood or urine, rectal or vaginal examination and the use of the diagnostic catheter will usually establish the diagnosis. Cysto-urethrography, cystoscopy and cystometry may supply confirmatory evidence, are usually not required, and may be contraindicated.

When the diagnosis of rupture of the urethra, bladder or ureter is in doubt, drain, divert the urinary stream, control bleeding, and repair the defect if practicable. The scalpel is still the safest instrument in urologic emergencies.

The following case reports are of patients wounded or injured on far-flung battle fronts, who received their first treatment in emergency stations and evacuation hospitals. The fact that they are alive is evidence of the effectiveness of their initial treatment. It would seem profitable to critically evaluate their surgery in respect to the four cardinal principles involved—drainage for extravasation, diversion of the urinary stream, hemostasis, and repair of the defect.

Case 1—A 26-year-old soldier, wounded on April 23, 1943, by a machine-gun bullet, had the wound of entrance just above the left greater trochanter, the wound of exit six centimeters above the right trochanter. The missile perforated the rectum, the urinary bladder, and injured the right sciatic nerve. Debridement of the wounds was carried out. At celiotomy, two sigmoid perforations and one of the ileum were sutured, two bladder perforations were closed, and the urine was diverted by cystostomy. He was transferred to an evacuation hospital and then to a station hospital where the suprapubic tube was removed on May 10, 1943. Following removal to a general hospital on May 14, 1943, he developed intestinal obstruction, and the diagnosis of vesico-enteric fistula was made. The suprapubic tube was reinserted and a transverse colostomy was performed. He was transferred to the Zone of the Interior and was admitted to Walter Reed General Hospital on September 16, 1943. Urine was draining through the cystostomy and from the wound over the right hip. He had a foot-drop on the right but the major part of the sciatic nerve was uninjured. The colostomy was functioning well. The vesico-enteric fistula had apparently healed. Intravenous urograms showed a moderate right hydronephrosis, with dilatation of the ureter down to a point near the bladder. A roentgenogram taken after injection of diodrast through an ureteral catheter passed through the sinus tract near the right greater trochanter, showed the right ureter dilated below an obstruction at the brim of the true pelvis.

* Read before the Fifty-sixth Annual Session, Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

SEVERE PELVIC INJURY

There was calcification to the right of the bladder, due to deposition of urine salts (Fig 1)

On September 12, 1943, five months after injury, right ureterocystoneostomy was performed through a right lower quadrant muscle-cutting incision. The ureter was readily exposed on the surface of the peritoneum and freed to the scar near the bladder. The cut end of the ureter was dissected from the fistulous tract which communicated with the wound in the right hip. Anastomosis was carried out by a method very similar to the usual technic of ureterosigmoidostomy. The bladder was perforated with an



FIG 1



FIG 2

FIG 1—Case 1. Preoperative roentgenogram showing urethral catheter in place, calcification in a fistulous tract behind the ureteral bladder, the bladder itself distended with air. An ureteral catheter is shown passing through the fistulous tract above the right trochanter. The lower portion of the right ureter is dilated with contrast media injected through the ureteral catheter.

FIG 2—Case 1. Postoperative excretory urogram showing excellent function of both kidneys. The bladder is irregular in shape, distended with iodide. Lipiodol is noted in the fistulous tract in front of the right ilium.

Halsted clamp at a point of fixation to the scar. A mattress suture of No. 1 chromic catgut was placed through the tip of the ureter which had been cut obliquely, the two ends of the suture were placed on two curved needles, passed through the cystostomy opening together and brought out three centimeters below the perforation to fix three centimeters of ureter inside the bladder. Three chromic catgut sutures were used to fasten the ureteral wall to the outer bladder wall. The wound was closed with drainage.

Intravenous urograms six weeks after operation showed that the hydronephrosis had been relieved and the kidney was functioning normally (Fig 2). On December 3, 1943, the wounds of the hips which communicated with each other and with the old suprapubic wound were curetted, and large amounts of scar tissue and calcified material were excised. The bladder wounds had healed, and the patient was voiding all of his urine through the urethra. On January 4, 1944, the colostomy was closed.

DISCUSSION—Critical evaluation of this case shows that the diagnosis of rupture of the right ureter was not made, because of inadequate exposure and drainage of the perforation on the right side of the bladder. Diversion of

urine from the bladder was adequate but due to diagnostic difficulty urine from the right kidney was allowed to drain through the débrided wound of the right thigh. Hemorrhage was controlled. Ureterocystoneostomy at the time of exploration would have prevented the formation of a fistula and also the deposition of calculus in the extravasated wound. The patient has made a satisfactory recovery after four major operative procedures.

Case 2—A 2nd Lt, A N C, was injured when a "jeep" in which she was riding overturned on August 19, 1944. She suffered fracture of the pelvis with remarkable separation of the symphysis, fracture of the right pubis into the acetabulum, with dislocation of the right hip. She was taken to a station hospital in severe shock, received morphine and plasma. She was placed in a plaster encasement temporarily because the dislocation of the right hip could not be reduced. After passage of a diagnostic catheter and draining 200 cc of blood from the bladder, 100 cc of skiodan was injected, and roentgenograms taken. These films were read as showing no evidence of extravasation, however, review of these films definitely indicates intraperitoneal extravasation of iodide (Fig 3). Because of negative roentgenographic evidence her bladder was not drained, in spite of positive signs of hematuria and perivesical mass felt by vaginal examination.

On the second day after injury cystoscopy was carried out and definite evidence of rupture was seen of the posterior wall of the bladder. Another cystogram was done which was also read as negative. Review of this film, again, shows peritoneal extravasation (Fig 4). The patient remained in a state of shock, there was extraordinary distention, peristalsis was absent, there was tenderness around the umbilicus, the patient was considered in too poor shape to stand surgery. She had a severe chill. Supportive treatment was continued.

On the third day after injury, suprapubic incision was made and extravasation of urine and blood found around the bladder and in the peritoneal cavity. Cystostomy was performed, fluid was evacuated from the peritoneal cavity, and perivesical drains placed. She had a good deal of fever for two weeks. Penicillin was administered. The cystostomy tube was removed on the 12th day and an urethral catheter placed.

Twenty-three days after injury it was noted that there was edema and induration about the right vulva. She was transferred to a General hospital where reduction of the hip was carried out under general anesthesia and a new spica applied.

On arrival at Walter Reed General Hospital on October 14, 1944, patient was wearing a hip spica, the hip dislocation had been reduced, the right pubic bone was in better position, but there was still marked dislocation at the acetabulum and wide separation of the symphysis pubis. The suprapubic wound had healed. She was suffering from severe pain on urination, referred to the left hip. There was gross pyuria.

Excretory urograms showed normal kidneys and ureters. The bladder was ovoid. On urination, iodide seemed to pass in the vulva tissues to the right of the bladder (Fig 5). The perivesical abscess produced by the extravasation finally pointed in the right vulva and was drained. The tract communicated from the perivesical space through the tissues behind the fractured pubis with the incision in the right vulva. Following this drainage the patient's temperature returned to normal and her condition rapidly improved. The bladder wound healed first, followed by the drainage tract behind the dislocated pubic bone.

DISCUSSION—The critical condition of the patient at the time of injury made surgical treatment hazardous. However, her condition did not improve by delay in initiating treatment for a ruptured bladder in order to obtain confirmatory evidence of rupture. Drainage of the prevesical extravas-

SEVERE PELVIC INJURY

FIG 3



FIG 4



FIG 5

FIG 3—Case 2 Cystogram taken at the time of injury, showing well filled bladder and extravasation of iodide into the perineum in the pelvis

FIG 4—Case 2 Cystogram taken two days after injury, showing partially distended bladder and iodide free in the peritoneal cavity. Dislocation of the right hip, fracture of the right pubic bone into the acetabulum, and wide separation of the symphysis pubis are noted

FIG 5—Case 2 Urethrogram taken during voiding. The pear shaped bladder is slightly irregular on the right side. The urethral orifice is open and extravasation of iodide can be seen behind the right pubic bone, extending into the right vulva

ation was inadequate. Diversion of urine was accomplished, hemostasis obtained, and the defect in the bladder which communicated with the peritoneum was sutured. The use of penicillin probably did have profound effect upon her peritonitis and perivesical infection. It did serve to wall off the prevesical abscess, which pointed and was drained seven days after penicillin was discontinued.

Case 3—A 27-year-old sergeant in the infantry, while on duty in the Southwest Pacific, suffered a crushing injury of the pelvis, amputation of his left leg at the thigh, severe crushing injury of the abdominal contents, and rupture of the bladder and membranous urethra, when an ammunition truck overturned. The patient was treated effectively for shock, his leg was amputated by the guillotine method, his bladder was drained suprapubically and he was sent to the nearest evacuation hospital. There an attempt was made to unite the ends of the urethra by passage of a catheter after sounds passed antegrade and retrograde had met in the region of the prostatic apex. With this catheter in place cystostomy drainage was maintained for some time, but when the suprapubic tube was removed no drainage of urine occurred through the urethral catheter.

The patient was admitted to Walter Reed General Hospital, three months after his initial injury, wearing a suprapubic tube. The urethral catheter was in place but drained no urine. On his arrival the cystostomy wound was dilated to allow introduction of the examining finger into the bladder. The urethral catheter did not pass through the prostatic urethra but entered the suprapubic wound through the space of Retzius. Roentgenograms showed the catheter to pass to the left of the midline, and to lay lateral to the prostate where it could be palpated by rectum.

Under sodium pentothal anesthesia, cystoscopy was carried out by passing the panendoscope through the cystostomy opening. Filiforms and catheters were admitted through the vesical orifice but would not pass for more than two centimeters. The cystoscope was removed and an attempt was made to pass sounds through the prostatic urethra retrograde to meet a sound passed antegrade. This maneuver failed.

On July 20, 1944, the operation, as described by Young, was undertaken through the perineum. There was no difficulty in anastomosing the prostatic apex with the torn end of the membranous urethra. Drainage was established in the prevesical space, from which considerable granulation tissue was curetted. A No. 24 Foley bag catheter was used as an urethral splint.

Nine days after operation a periurethral abscess at the penoscrotal juncture was drained. On the 10th day a severe secondary hemorrhage occurred which required packing of the prevesical space and the perineum. At that time the sutures in the perineum had sloughed out and there was a two-centimeter defect in the urethra at the prostatic apex. This was resutured on the 18th day, when there was slight hemorrhage from the perineum. Traction was made on the Foley bag to relieve strain on the suture line.

Twenty-three days after operation the patient had another severe hemorrhage which required opening of the suprapubic wound, packing of the prevesical space, and packing of the perineum and the area of the periurethral abscess. There was severe sepsis of the entire wound. To obtain hemostasis the defective membranous urethra was again sutured. Severe secondary hemorrhage again occurred on the 37th day, after two weeks of cessation of all bleeding, and required packing of the entire area in front of the prostate and urethra.

DISCUSSION—The patient had adequate drainage, diversion of the urinary stream, and hemostasis. Repair was not immediately undertaken because of

the precarious condition of the patient. Later attempted establishment of urethral continuity was unsuccessful. A false passage was established. It seems probable that perineal repair of the defect was undertaken too soon after removal of the catheter from the false passage. Secondary hemorrhage is a serious complication in many of our severely wounded. Scar, infection, and a debilitated patient are a poor surgical combination. Recently we have been able to satisfactorily repair the defects.

Case 4—A 40-year-old gunner of a B-17 bomber was struck by a 20-mm cannon shell, September 27, 1943. Major Herbert Willey Meyer's notes are quoted: "There is a large wound of the anteromedial aspect of the left thigh extending from 10 cm above the knee to the inguinal region, damaging and destroying the muscles of the thigh, the abductor group and the sartorius. The femoral vessels are exposed from Poupart's ligament to the midthigh but are still in their sheath. The skin of the left scrotum is destroyed, the left testicle practically destroyed. The right scrotum is intact. The perineum is extensively damaged. There is a strand of tissue eight centimeters long and one centimeter wide, attached to the Corpora of the penis and showing some urethral mucosa. The entire urethra is divided from the exposed prostate in the bulbous portion of the corpus spongiosum. The entire perineal body is destroyed. The skin around the anus is completely avulsed from the anal canal. There is a wound of the right buttock continuous with the perineal wound, from which there is a steady oozing of blood. This wound leads along the descending ramus of the pubis and ischium to the posterior aspect of the neck of the femur where a large metallic foreign body can be felt. The inferior pubic ramus and the ischium are fractured. Many loose pieces of bone are in the tract."

A rapid colostomy was performed through a McBurney incision. The peritoneum was not sutured. A rubber catheter was placed under the loop for support and the external oblique fascia was closed above and below the loop. Suprapubic cystostomy was performed. The wound of the left thigh was excised. The left testicle was removed and the scrotum debrided. The perineum was debrided and a No. 14 F catheter was placed through the urethra. The wound of the right buttock was débrided. Penicillin therapy was instituted and later the wound of the left thigh was grafted.

This patient was evacuated to the Zone of the Interior and was admitted to Walter Reed General Hospital February 27, 1944.

On March 30 plastic repair of the urethra was undertaken. With the patient in the lithotomy position it was impossible to abduct the left thigh because of scar formation above the grafted area. Relaxing incisions were made in the scar at the left groin so that exposure of the perineum was effected. A sound passed through the anterior urethra was obstructed just behind the penoscrotal juncture. Incision was made over the tip of the sound. By dissecting around the urethra it was possible to bring the penis and urethra backward about three centimeters. Filiforms and followers entered the bladder through the prostatic urethra. By means of an inverted U-incision the rectum was brought forward to its normal position in the perineum. By exploring in the wound of the right buttock, mucous membrane was discovered and turned to cover the remaining defect in the urethral bulb. A large shift of the skin of the right buttock was utilized to cover the newly made urethra. This procedure left a sizeable defect over the buttock behind the ischium. There remained a large defect in the region of the left scrotum. These were covered with petrolatum gauze. A No. 26 Foley bag catheter was used as a splint for the urethra. The cystostomy was left open, with a No. 32 Malecot catheter in place.

A small urethral perineal fistula persisted for six weeks and finally healed. The only complication was the formation of two calculi in the urethra (Fig. 6). One was removed.

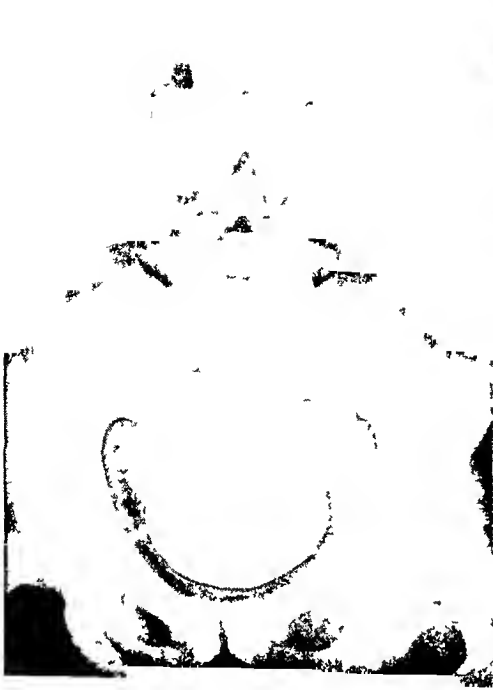


FIG 6



FIG 7

FIG 6—Case 4 Cystogram showing perfectly normal bladder and closed vesical orifice. There is marked dislocation of the fragment of ischium. A calculus may be seen in the bulbous urethra.

FIG 7—Case 4 Postoperative cystourethrogram during voiding. The posterior urethra and bulbous urethra are filled with iodide. Note that the normal constriction at the external upper sphincter is lacking.



FIG 8



FIG 9

FIG 8—Case 4 Postoperative result after urethroplasty, showing grafting scar of the left thigh, well-healed suprapubic wound and closed colostomy wound.

FIG 9—Case 4 Postoperative result after urethroplasty, showing scar of the right buttock, perineum and left thigh. The left scrotum has been resected. Wounds are well-healed. Patient's bladder and bowel control are perfect.

through the fistulous opening, and the other was removed by means of ureteral stone forceps, through the anterior urethra (Figs 7, 8 and 9) After the urethra had completely healed and the patient was voiding normally, the colostomy was closed The urethra has been dilated to No 26 F

DISCUSSION —Extravasation was prevented and diversion of the urinary stream accomplished by early cystostomy Hemostasis, a serious problem, was controlled by sutures and packing Repair of a large defect in the urethra was accomplished after sufficient time had been allowed for wound healing and contracture of scar Conservative emergency surgery and the use of every available tissue has enabled us to gain a very satisfactory result It should be noted that in spite of loss of external sphincter and practically all of the perineal and bulbar musculature, normal urination is reestablished

CONCLUSIONS

The soundness of the four surgical principles for treatment of ruptures of the bladder, urethra and ureter, is established Drainage for the prevention of or treatment of existing extravasation is immediately imperative to save life and lessen morbidity Diversion of urine is essential Hemostasis in severe war wounds may be a serious problem Repair of defects is desirable at the time of initial surgery, to allow healing with minimum scar formation If repair is impracticable at the time of injury, sufficient time should be allowed for healing, scar contracture, subsidence of infection and for rehabilitation of the patient, before definitive surgery is undertaken Several patients with severe pelvic injury, complicated by rupture of the bladder and membranous urethra who had repair of defects performed at the time of injury, have been observed by us and the results have been extremely satisfactory We have also carried out perineal repair of the ruptured membranous urethra on seven patients who had had drainage and cystostomy in whom it was impracticable to carry out repair at the time of injury, with satisfactory results It should be pointed out, however, that delayed repair results in more scar formation Therefore, early repair is preferable whenever possible

STUDIES ON TRAUMATIC SHOCK

V—THE TREATMENT OF CLINICAL SHOCK WITH GELATIN*

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EVEN before the outbreak of the present war, considerable interest had developed in blood substitutes, other than plasma or serum albumin, for the treatment of traumatic shock, among the list of materials suggested for this use was gelatin

The pertinent literature on this subject, has been reviewed thoroughly in two excellent papers which have appeared recently from the University of Pennsylvania Surgical Clinic^{1,2} Studies carried out by these workers have shown that specially prepared ossein gelatin can be given intravenously to human patients without fear of adverse pyrogenic antigenic, hepatic or renal reaction A rather large clinical experience during the past three years has increased our desire, and confirmed our impression, of the need for a useful substitute for plasma or albumin in the treatment of clinical shock After conversations with Doctors Lockwood and Koop, we undertook to treat with gelatin infusions a number of patients suffering from shock due to trauma, blood loss, or extensive burns

The present communication, therefore, is concerned with the effectiveness of gelatin in the treatment of 67 patients in shock because of trauma to the extremities, chest and abdomen, and 28 severely burned patients, where gelatin has been used almost solely as the initial intravenous therapy fluid Illustrative case reports are given for each different group of patients

MATERIALS AND METHODS

Gelatin for intravenous use is prepared by hydrolysis, enzymatic or chemical, if certain well defined precautions are observed in its preparation, a product of rather unusual uniformity as regards viscosity and molecular homogeneity can be obtained Through the cooperation of the Blood Substitutes Committee of the National Research Council and the gelatin industry, a considerable body of evidence on the physicochemical properties of gelatin has been obtained in the past two years These studies have made it clear that for intravenous use not "any" gelatin solution will suffice For this reason, the Food and Drug Administration has laid

* This study was carried out under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Medical College of Virginia

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down specific requirements for gelatin solutions when they can be made available for general use

The molecular weight of gelatin varies according to the amount of degradation it has suffered in its preparation. Whereas serum albumin has a molecular weight of about 69,000, that of "lightly degraded" gelatin is around 35,000, and "heavily degraded," about 20,000

The effectiveness of any plasma substitute in the treatment of shock naturally depends to a large extent on the time it remains in the blood stream, and this is dependent on molecular size. Dr. D. Tourtelotte* supplied us with two types of gelatin solution, the "lightly" and "heavily degraded" (designated as P-20 and P-180). The first preparation had been degraded by autoclave treatment at 15 pounds for 20 minutes (P-20), and the second by autoclave treatment for 180 minutes (P-180).

TABLE I
RETENTION OF GELATIN P-20
' Lightly Degraded

Name	Hour	Plasma Volume Cc	Hematocrit	Protein Conc %	Total Circulating Protein Gm	Gain Protein Gm	Notes
A W	0	2099	48	6.8	143		Given 1000 cc P-20 6.0% gelatin (60 grams)
	4	3214	41	6.6	212	+69	
	8	3189	42	6.7	214	+73	
E L	0	2539	50	7.5	189		Given 1000 cc 6.0% P-20 gelatin (60 grams)
	4	3620	44	7.2	261	+72	
	8	3833	45	7.2	277	+88	

CLINICAL SHOCK OBSERVATIONS

Gelatin has been given to 67 patients in moderate or severe shock due to the various causes listed in Table III. The "acute blood loss" group includes those patients who have suffered lacerations of large vessels from knife or razor wounds, with subsequent loss of large amounts of blood. The "chest injury" group is made up of patients in shock from penetrating wounds of the chest, causing injury to such vessels as the intercostal and internal mammary arteries, pulmonary vessels, and three patients with stab wounds of the heart. The "abdominal injury" group comprises those patients who have suffered stab and gunshot wounds of the abdomen, or a ruptured viscus from direct trauma, in the "skeletal trauma" group are patients in shock from simple and/or compound fractures of the long bones or pelvis, or traumatic amputations of the lower extremities. Blood volume determinations and hematocrit estimations were made on many of these shock patients. That shock was due in the main to the decreased circulating blood volume.

* We are grateful to Dr. D. Tourtelotte and the Chas. B. Knox Gelatin Company for liberal supplies of these solutions for clinical treatment.

(usually 30-40 per cent) was borne out by these laboratory investigations and also by the recovery from the serous cavities of large quantities of whole blood in many of the operated cases. We have been conducting, therefore, a clinical study of the efficacy of one particular gelatin solution in the alleviation of clinical shock of the type that is most important and interesting to practicing surgeons, civilian and military.

From each of these groups of shock patients has been selected a representative case. In the accompanying clinical record and clinical charts is shown the response of these shock patients to intravenously infused gelatin, usually in 500-1000 cc amounts.

TABLE II
RETENTION OF GELATIN P-180
* Heavily Degraded

Name	Hour	Plasma Volume Cc	Hematocrit	Protein Conc %	Total Circulating Protein Gm	Gain Protein Gm	Notes
C C	0	2075	44	7.1	147		Given 1000 cc 6% P-180 gelatin (60 grams)
	4	2343	42	6.6	155	+8	
	8	2102	44	6.9	145	-2	
W M	0	2295	41	8.3	191		Given 1000 cc 6% P-180 gelatin (60 grams)
	4	2730	37	7.5	205	+14	
	8	2150	42	7.8	168	-23	

Initially, each of these gelatin preparations were given intravenously to four convalescent patients, and their disappearance rates followed by the determination of plasma volume before, and at intervals after, the rapid infusion of 1000 cc of a six-per cent gelatin solution in 0.85 per cent saline. From Tables I and II it can readily be seen that the heavily degraded gelatin leaves the blood rapidly, while in contrast, in the normal patient, most of the lightly degraded gelatin is still present in the blood stream at the eighth hour after rapid infusion. Similar retention of lightly degraded gelatin was noted in the studies of Parkins, *et al*.¹ On the basis of these preliminary studies, we selected the less degraded gelatin for further clinical studies, in this paper is reported our experience in clinical shock from the use of this particular gelatin preparation.

It has been our practice generally to give gelatin infusions (as well as plasma or whole blood) by the "rapid syringe technic" which employs a small syringe attached to the tubing set-up by a three-way stop cock (Fig. 1). Only by this technic has our shock group found it possible to restore rapidly and adequately the circulating blood volume of many severely shocked patients. We are certain that some lives have been saved by this method of rapid infusion that otherwise would have been lost if more time-consuming infusion technics had been used.

ACUTE BLOOD LOSS

Case 1 (Fig 2)—*Diagnosis* Multiple lacerations of face and scalp, including left temporal artery, hemorrhagic shock

B D, a 42-year-old white male, was admitted to hospital, February 6, 1944, after an automobile accident. When taken from car by the ambulance surgeon he was bleeding



FIG 1—Set up for rapid intravenous infusions for use with whole blood, gelatin, or plasma

1 An ordinary 750 cc bottle, 2 a 10 or 20 cc Luer Lok syringe. These size syringes are much more efficient for rapid infusion than the longer 50 cc size, 3 A three way stop cock, a 16 or 18 gauge needle.

Our shock group has experimented with practically all types of equipment designed for infusing fluids rapidly in shock, and have found the set up herein described by far the most efficient.

profusely from long lacerations of the left face and scalp, especially from a severed temporal artery. On admission to emergency room, the blood pressure was 60/40, pulse 72, respiration 26. Patient was not alcoholic. Initial hematocrit 40 per cent. An immediate rapid infusion of 1000 cc gelatin solution restored the blood pressure to

TABLE III

SHOCK PATIENTS TREATED WITH GELATIN

	No of Cases
Acute blood loss	15
Chest injury	14
Abdominal injury	10
Skeletal trauma	28
Severe burns	28

110/70 and then to 170/80. The hematocrit at the end of two hours was 32 per cent. After suturing of wounds and four days hospitalization, recovery was complete except for a secondary anemia (Hb 72 per cent).

Case 2 (Fig 3)—*Diagnosis* Gunshot wound of left groin, severance of left femoral artery, severe hemorrhagic shock. *Operation* Ligation of left femoral artery and vein, gelatin infusion for shock.

Acute Blood Loss

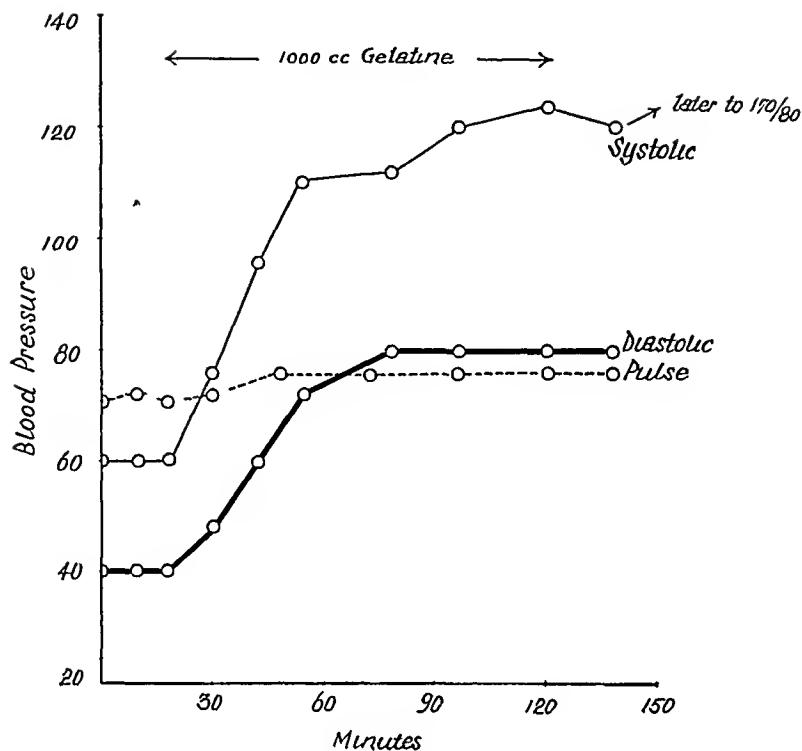


FIG 2—Clinical effects of gelatin infusion in acute blood loss from multiple lacerations

Gun Shot Wound of Artery

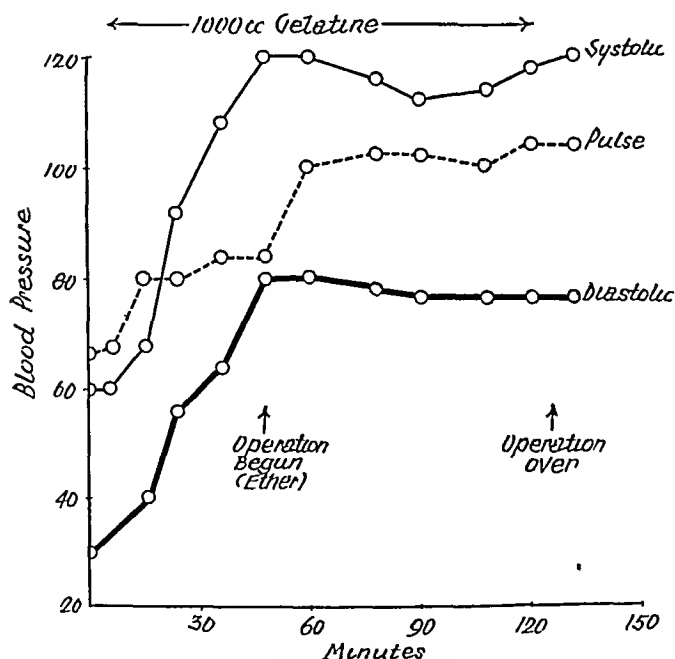


FIG 3—Clinical effects of gelatin infusions in acute blood loss from a severed femoral artery

GELATIN IN SHOCK

G F, a 50-year-old colored male, was shot at close range with a 32-caliber revolver. On admission to St Phillips Hospital emergency room, the patient's blood pressure was 60/30, pulse 65, extremities cool and dry, no sweating, venous filling fair. Plasma volume estimation—32 cc/Kg, hematocrit 41 per cent, representing loss of 1400 cc whole blood. There was a bullet wound immediately over the femoral artery.

STAB WOUND OF HEART

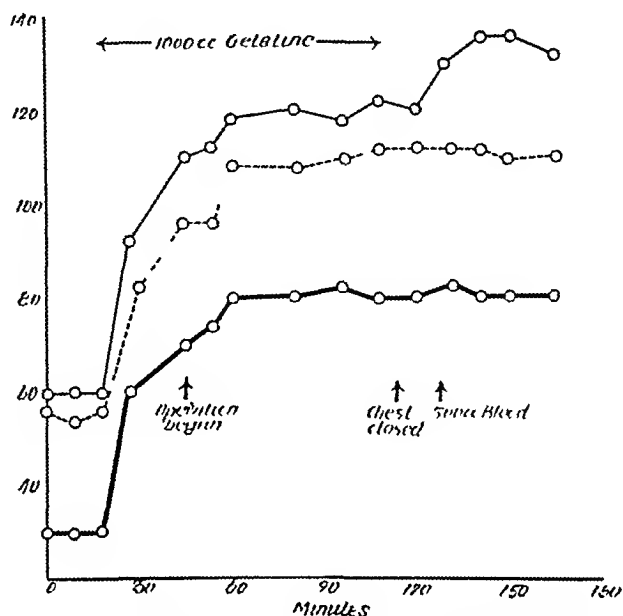


FIG 4—Clinical effects of gelatin infusions in a patient with stab wound of right auricle

Stab Wound of Chest

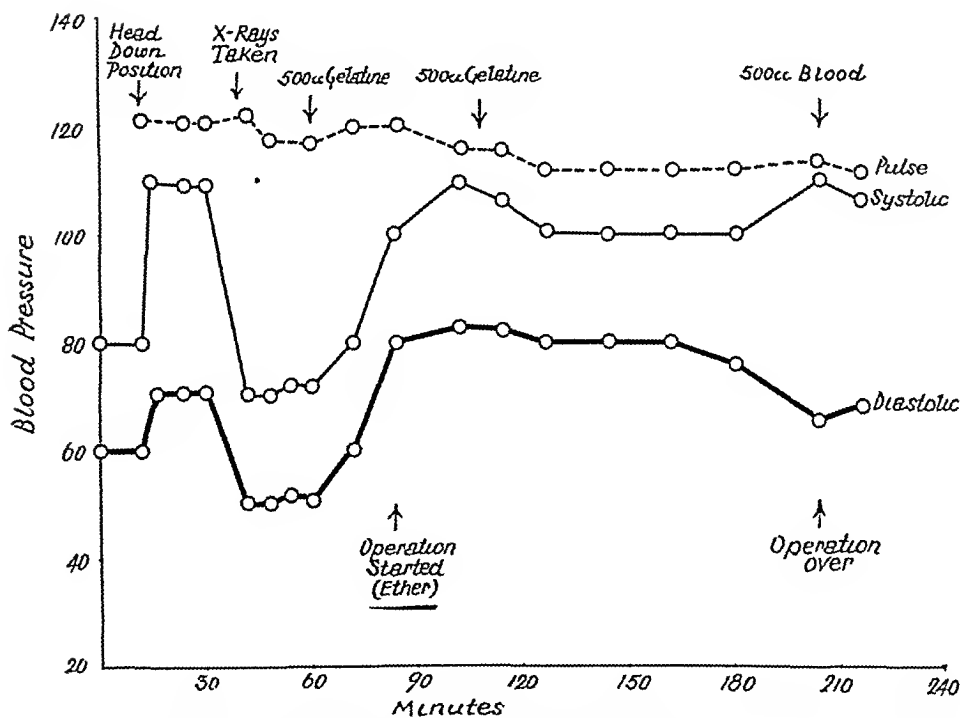


FIG 5—Clinical effects of gelatin infusions in a patient with stab wound of the chest severing an internal mammary artery

at Poupart's ligament, with no pulsation below of this or the popliteal artery. A rapid infusion of gelatin restored the blood pressure to 120/80, and this was maintained during the operation that followed by the infusion of another 500 cc gelatin solution. A transfusion of 500 cc whole blood was given after the operation to combat anemia (Hemoglobin had fallen to 62 per cent). Two novocaine lumbar sympathetic blocks were carried out during the night, and despite the fact that the continuity of the artery could not be restored, the patient made a good recovery.

Figure 3 shows the effect of gelatin infusions in this shock patient.

CHEST INJURY

Case 3 (Fig 4)—*Diagnosis* Stab wound of right auricle, "sucking" hemopneumothorax, secondary shock. *Operation* Cardiorrhaphy.

V S, a 28-year-old colored female, had been stabbed in the right chest while asleep in bed. On admission to the St Phillips Hospital not long after, she was in a state of profound shock, blood pressure 60/30, extremities cool and dry, pulse 56, of extremely poor volume at the wrist. There was a stab wound 2 cm in length in the second right interspace, 1 cm from the sternal border. A diagnosis of stab wound of the heart or severance of the right internal mammary artery was made. Plasma volume was 35 cc Kg, hematocrit 37 per cent. Patient was prepared for operation and given by rapid infusion 500 cc gelatin solution. After 300 or 400 cc had been given the blood pressure rose to 110/70, pulse 90. Patient was taken to operating room, where a second 500 cc gelatin infusion was started. At operation, a large amount of blood was found in the right pleural cavity, coming from a 1-cm stab wound of the right auricle through a rent in the pericardium. This was closed with some difficulty because of the friable nature of the tissue, but the patient withstood the operation quite well, as can be seen from Figure 4. Nine hundred cubic centimeters of whole blood was collected from the right pleural cavity and given to the patient by autotransfusion.

Case 4 (Fig 5)—*Diagnosis* Stab wound of the left chest, severance of left internal mammary artery, hemorrhagic shock. *Operation* Exploratory thoracotomy, ligation of left internal mammary artery and vein, gelatin infusion.

J J, a 22-year-old colored male, had been stabbed in the left chest one hour before admission. On entry, he was in moderate shock, blood pressure 80/60, extremities cold and dry, pulse 76. When placed in the Trendelenburg position, blood pressure rose to 110/70. There was a 2-cm stab wound in the left second interspace in the parasternal line. A diagnosis of severed internal mammary artery was made and patient taken to the operating room. On arrival there, due to the fact the patient had been allowed to raise his head, his blood pressure had fallen to 70/50. Five hundred cubic centimeters of gelatin solution was given rapidly and the pressure rose to 100/80, and the operation was started while the second 500 cc of gelatin solution was being given slowly. At operation, about 1500 cc whole blood was found in the left pleural cavity, coming from a severed left internal mammary artery, which was ligated. No other intrathoracic injury was found. Figure 5 shows the response of this patient to 1000 cc gelatin infusion. Five hundred cubic centimeters of whole blood was given by autotransfusion after the operation (1000 cc was lost by clotting).

ABDOMINAL INJURIES

Case 5 (Fig 6)—*Diagnosis* Gunshot wound of abdomen (liver, stomach and spleen), severe secondary shock. *Operation* Exploratory celiotomy, splenectomy, and closure of stomach wounds, gelatin infusion for shock.

R T, a 21-year-old male, sustained a self-inflicted gunshot wound of the abdomen (38-caliber revolver). On admission there was a wound of entrance in the left upper quadrant of the abdomen, and a wound of exit in the left loin. Blood pressure initially 120/80, and fell to 80/60, pulse 78, respiration 20, extremities cool and dry. Plasma

Gunshot Wound of Abdomen

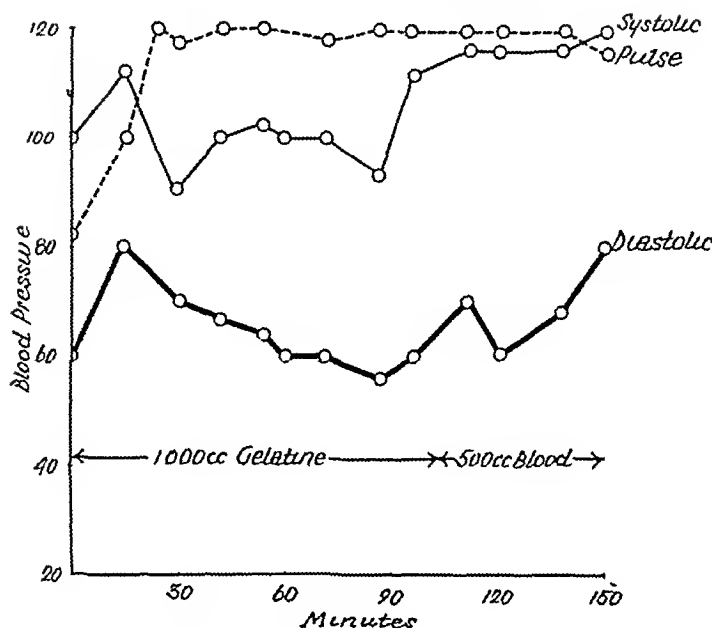


FIG 6—Clinical effects of gelatin infusion in a patient with gunshot wound of the abdomen, involving the liver, stomach, and spleen

Gun Shot Wound of Abdomen

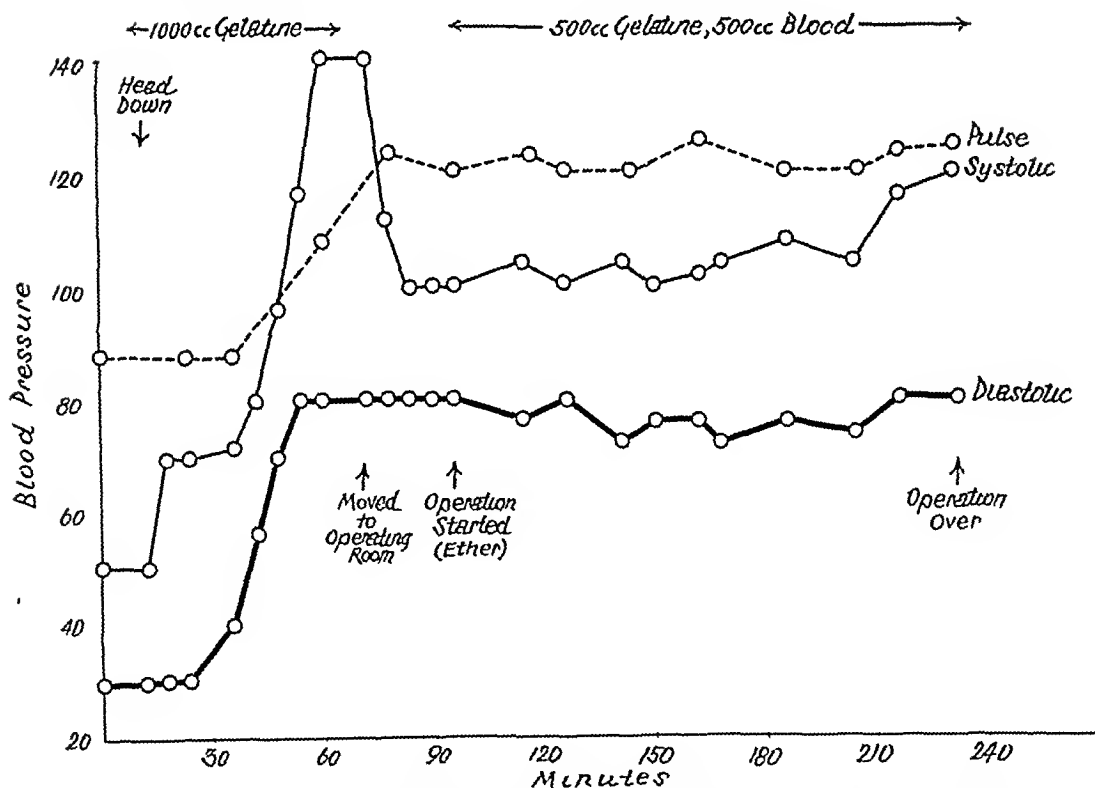


FIG 7—Clinical effects of gelatin infusions in a patient with gunshot wound of the abdomen, with severe hemorrhagic shock

volume 33 cc /Kg, hematocrit 42 per cent, representing a blood loss of approximately 1500 cc. The patient was taken to the operating room and given 1000 cc gelatin solution, followed by 500 cc whole blood at the close of operation. At celiotomy, 1800 cc whole blood was collected. There was a through-and-through wound of the left lobe of liver, a through-and-through wound of the stomach, and a perforation of the upper pole of the spleen, from which blood was issuing. Splenectomy and repair of the stomach wounds were performed. Figure 6 illustrates the operative course of this patient.

Bilateral Traumatic Thigh Amputation

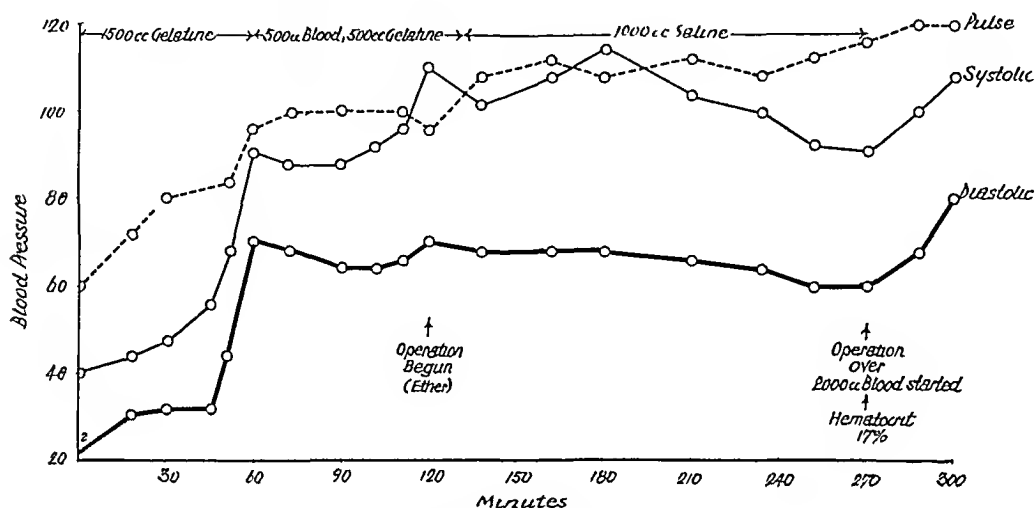


FIG 8—Clinical effects of gelatin infusions in a patient with bilateral traumatic amputations of thighs

Bilateral Fracture of Hip

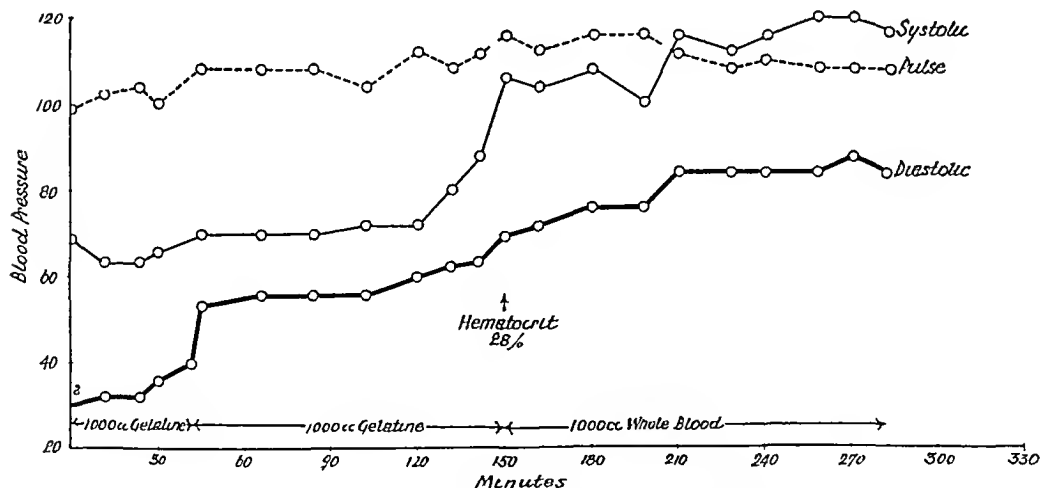


FIG 9—Clinical effects of gelatin infusions in a patient with bilateral fractures of hips

Case 6 (Fig 7)—*Diagnosis* Gunshot wound of abdomen, perforation of jejunum, severe hemorrhagic shock. *Operation* Exploratory celiotomy, closure of jejunum.

G E S, a 44-year-old white male, had been shot with a 22-caliber rifle at close range. When seen in the emergency room not long after (30 minutes), he was in a state of profound shock. Blood pressure 50/30, pulse 88, extremities cold and wet with perspiration. Skin bloodless, he was placed in Trendelenburg position, with blood

pressure rising to 70/30. He was given, by rapid intravenous infusion, 1000 cc gelatin, and after 40 minutes, when he was taken to the operating room, his extremities had become warm and dry, the blood pressure had risen to 140/80. On opening into the peritoneal cavity, a large amount of free blood was encountered, there were four small openings in the jejunum, which were closed by appropriate measures. There was found an enormous left retroperitoneal hematoma extending from the pelvis to the left renal area. A stab wound was made in the left loin into the hematoma zone.

The patient withstood the operation fairly well, as can be noted from Figure 7. However, about 14 hours after the operation, when he was thrashing about the bed, he suddenly collapsed and died before an intravenous infusion could be started. Necropsy showed a severance of the left internal iliac artery in the pelvis, from which the hemorrhage had occurred.

SKELETAL TRAUMA

Case 7 (Fig 8)—*Diagnosis* Bilateral traumatic amputation, thighs, severe traumatic shock. *Operation* Revision of amputation, suprapubic cystotomy, gelatin and blood infusions.

R C S, a 34-year-old white male, was run over by a street car. On examination soon after in the emergency room, it was noted that there was a severe crushing injury to both legs from above the knees downward. Tourniquets were applied above the zone of injury. The blood pressure was 40/0, pulse 60, poor volume. Patient was covered with profuse, cold perspiration. He was given 1500 cc gelatin solution, and blood pressure rose to 90/70. This was followed by 500 cc whole blood and 500 cc gelatin, the blood pressure rose to 110/70. He was taken to the operating room where, under ether anesthesia, a bilateral thigh amputation and suprapubic cystotomy was carried out. At the close of the operation, 2000 cc whole blood was given because after the patient had received 2000 cc gelatin, it was found that the hematocrit had fallen to 17 per cent. (This large whole blood infusion brought the hemoglobin from 35 per cent to 72 per cent). The patient recovered.

Case 8 (Fig 9)—*Diagnosis* Intracapsular fracture right hip, fracture dislocation, left hip, severe shock. *Operation* Deferred.

V W W, a 53-year-old white female, had been in an automobile accident close to Richmond. She was seen by us about 35 minutes after the accident. On admission, the extremities were cold and dry. The skin was very pale, blood pressure was 68/?, pulse 98, poor volume. Raising or lowering the head did not alter the pressure readings. One thousand cubic centimeters gelatin was given rapidly, but pressure rose only to 70/54. A second 1000 cc gelatin was then given, and gradually the blood pressure rose to 106/78. The hematocrit had by this time fallen from 40 per cent to 28 per cent, so the patient was given, by slow infusion, 1000 cc whole blood. In four hours, the blood pressure stabilized at 140/90. The plasma volume on admission was 32 cc/Kg, hematocrit 40 per cent.

SEVERE BURNS

To illustrate the effectiveness of gelatin solutions in the treatment of burn shock, we have chosen to present data on two severely burned children. It has been our experience that burn shock is apt to be very severe and difficult to treat in the child, even more so than in the adult. Our experience with the use of gelatin in burns includes now 28 severely burned patients. To show that we have been justified in calling these "severe burns," photographs of four of these patients are shown in Figures 10, 11, 12 and 13.

There has been no death from *burn shock* in this group of 28 patients, although two of this group died on the 12th and 16th day, respectively. One,

a child (Fig 10), died as a result of injudicious attempts at early removal of slough on the 16th day, the second, a 78-year-old man with a complete third-degree burn of one leg, died on the 12th day, presumably of congestive heart failure

All things considered, our experience with gelatin in the management of burn shock has been very satisfactory. Our present plan of management



FIG 10.—Photograph of posterior view of 11 year old severely burned child. The anterior portion of body was equally as badly burned. Burn shock was well controlled by gelatin infusions given every fourth to sixth hour during the first 48 hours.

is to reserve its use to the first 28-48-hour period when burn shock is most to be feared, and then give whole blood subsequently. From our experience with severely burned children, we now prefer to give fairly large infusions of gelatin at four- to six-hour intervals for the first 24-36 hours, if this is done, burn shock is usually avoided. These infusions are given even though the patient's appearance is good, and without regard for the hematocrit figures. If the burn is largely superficial (second-degree) and is widespread, it is our practice to give somewhat larger gelatin infusions during the "shock" period. Also, we almost routinely give quite large gelatin infusions (250-400 cc) to small children (3-4 years). In children, the infusions are given by

GELATIN IN SHOCK



FIG 11—Photograph (posterolateral view) of severely burned six year old child at time of first dressing on the 14th day. Burn shock was treated by gelatin infusions given every sixth hour during the first 36 hours



FIG 12—Photograph of severely burned child (E H Case 2, see text) at time of first grafting. Burn shock was severe in this child but was successfully managed by gelatin infusions

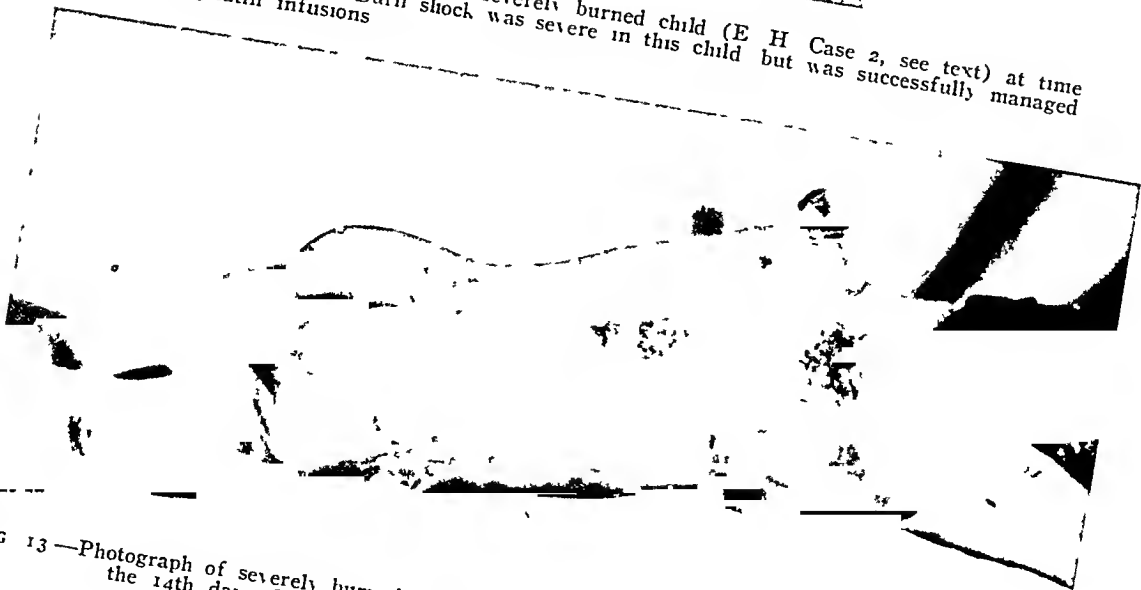


FIG 13—Photograph of severely burned child (C J Case 1, see text) at time of first redressing on the 14th day. Burn shock was successfully managed by gelatin infusions

the "rapid syringe" technic, and we have yet to note any evidence that would suggest overloading of the vascular system

Case 1 (Fig 14)—*Diagnosis* Severe burns of entire back, buttocks, upper thighs, face, and arms (second-degree)

C J, a five-year-old colored boy, was burned when a pail of boiling water fell on him from a stove. He was first seen about 15 hours after the accident. On admission,

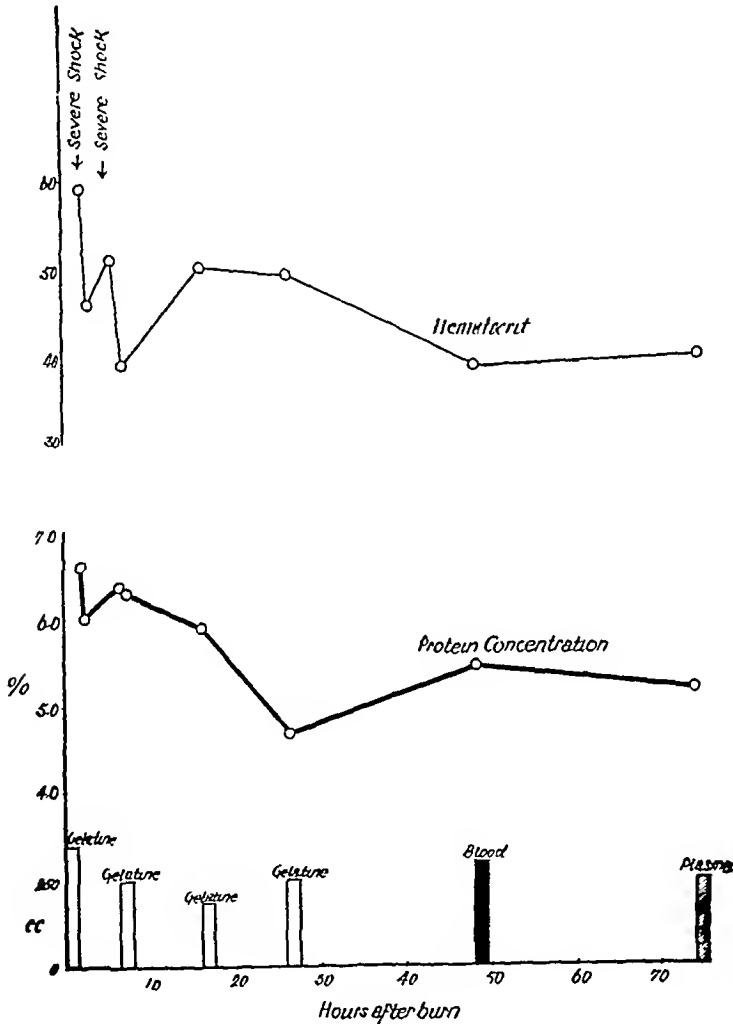


FIG 14—Chart illustrating the effects of gelatin infusions in a severe burn (Case 1, C J) in controlling hemoconcentration

the child appeared almost moribund, no pulse could be felt even at the femoral artery in the groin. Extremities were cold and dry. Initial hematocrit 59 per cent, total plasma protein 66 per cent. Child was given, by rapid infusion, 350 cc gelatin into femoral vein. In about ten minutes, child was alert, asking for his mother. Three hours later, although the hematocrit was only 51 per cent, the child was again in shock (cold extremities, very poor pulse volume) so he was given another 250 cc infusion of gelatin. (Blood analysis showed that no gelatin remained in blood stream of that given earlier). Subsequently, he was given additional gelatin infusions at the 16th and 26th hours. The child began to show clinical evidence of burn toxemia at about the 48th hour, but this had disappeared by the 6th day. The plasma protein

GELATIN IN SHOCK

dropped to 47 per cent on the 6th day, despite two blood transfusions and 250 cc plasma Figure 14 illustrates the course of treatment and response in this child

Case 2 (Fig 15)—*Diagnosis* Severe burns of entire right leg, right abdomen, and chest (third-degree)

E H, a small six-year-old white boy had his clothes catch on fire On admission, he did not appear to be in shock The burns were obviously third-degree in nature The

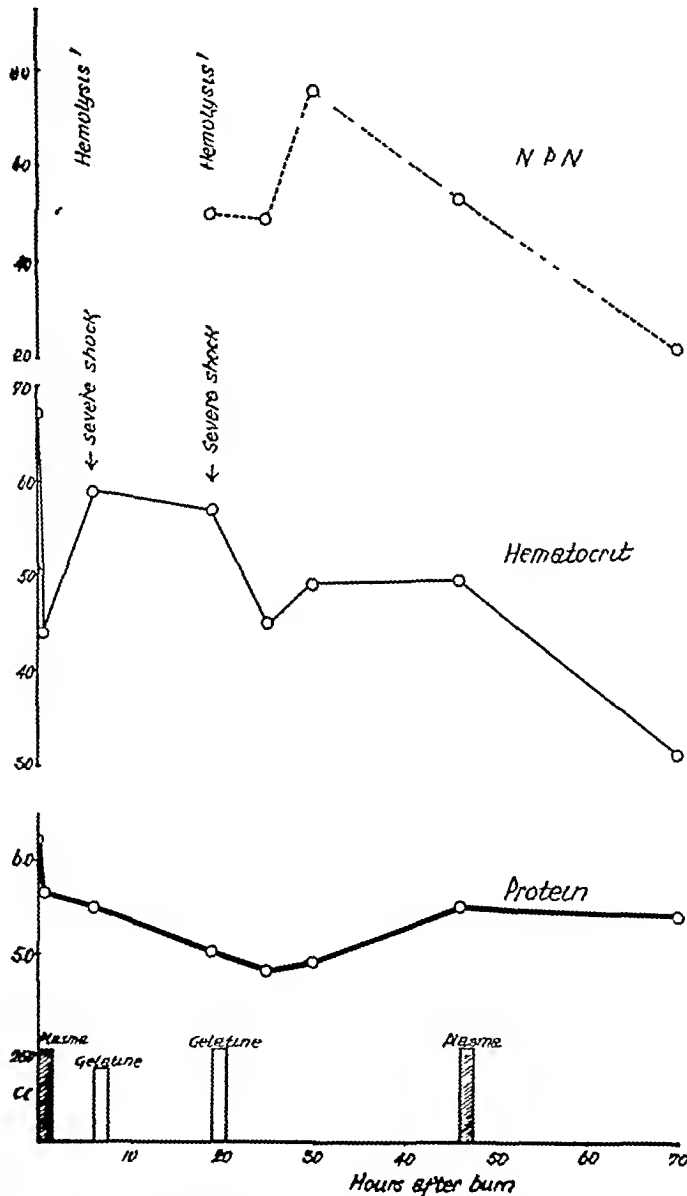


FIG 15—Chart illustrating the effects of gelatin infusions in a severe third degree burn (Case 2, E H)

ordinary sulfanilamide gauze pressure dressings were used, 250 cc plasma being given prophylactically About five hours later the child was in profound shock, the blood pressure 60/40, pulse 160, poor volume (Hematocrit on admission was 67 per cent, but had been brought to 44 per cent by the plasma infusion) Hematocrit at the fifth hour was 59 per cent, and the plasma showed definite signs of free hemoglobin Two hundred cubic centimeters gelatin was given by rapid infusion, the blood pressure immediately rising to 110/70, and the pulse fell to 120 Orders were left for the patient to receive 250 cc gelatin in six hours (during the night) but these were disregarded by the intern "because he looked so well" Early in the morning, the burn team was called because the patient

was again in shock (blood pressure 60/30, pulse 160), so he was given 250 cc gelatin by rapid infusion, to which he responded as before. No more gelatin infusions were given. After the third day, regularly, whole blood transfusions were given. Recovery was complete after five skin-grafting operations.

DISCUSSION

THE CLINICAL EVALUATION OF GELATIN FOR SHOCK THERAPY

It is our impression that our experience has now been sufficiently extensive and varied for us to evaluate the clinical value of gelatin solutions in the management of traumatic and burn shock.

ADVANTAGES

(A) One of the chief advantages in gelatin for the management of shock will be its ready availability when it can be supplied in large amounts. The plasma and whole blood program of the American Red Cross has been so eminently successful during the present war that there possibly has been no acute need for substitute. Should large and small hospitals alike experience difficulty in maintaining a steady supply of plasma after hostilities cease, we believe properly selected gelatin solutions will prove helpful in shock management, especially in those smaller centers where it is so difficult to secure plasma.

(B) When large scale production of gelatin solutions can be attained these solutions should be much less expensive than plasma, either desiccated or frozen.

(C) Intelligent use of gelatin infusions in centers where plasma banks can be operated, improves greatly the available supply of plasma. In our own blood bank, where an attempt is made to keep 600 bottles of frozen plasma on hand for emergency use, in the one month, when we were without gelatin this year, our frozen plasma stocks dropped to less than 400 bottles.

(D) From our experience, it is apparent that gelatin is especially indicated during the first 48 hours, since most infused fluid (plasma or gelatin) is lost into the burned area during this period. This results in a large saving of plasma.

(E) *Foreign Protein Reaction*—With our first supply of gelatin from Doctor Tourtelotte, we saw two moderately severe reactions, one patient showing severe cyanosis and dyspnea, the other moderate urticaria and itching. Since we have been supplied with gelatin solutions free of the preservative phenyl mercuric borate, there has been no instance of foreign protein reaction. Thus, the reactions with gelatin seem to be less frequent than one ordinarily experiences with carefully prepared pooled plasma. Also, we now see practically no venous thrombosis at the site of injection.

(F) Apparently, gelatin infusions can be given in the shock state when renal blood flow has practically ceased without deposition in the kidney. Doctors Phillips and Van Slyke³ have studied this problem extensively in a shock preparation consisting of an isolated single kidney, with the renal vessels clamped-off for four hours, and could find no evidence of renal damage.

from gelatin. The studies of Koop, *et al*,² demonstrate that gelatin has none of the serious hepatic effects seen when acacia solutions are used

(G) Although earlier we had feared the possible deleterious effects of large gelatin infusions on the clotting mechanism, prothrombin values seem to remain at normal levels even when as much as 2000 cc of gelatin solution has been given to patients in shock because of greatly reduced blood volume

DISADVANTAGES

(A) *Pseudo-agglutination*—It was earlier noted by Ivy, and his co-workers,⁴ that a serious pseudo-agglutination of erythrocytes occurred when gelatin solutions were given to dogs. This has greatly disturbed some observers, but it seems to have no serious consequences in our clinical experience. In a practical sense, the most serious effect of this reaction is to cause marked rouleaux formation during cross-matching after a patient has received an infusion of gelatin. Fortunately, this difficulty has now been obviated by Doctors Koop and Bullitt,⁵ who have demonstrated that if a drop or two of a 10 per cent glycine in physiologic saline is added to the erythrocyte-serum suspension (in the cross-matching procedure), this pseudo-agglutination of erythrocytes is abolished.

(B) *Viscosity*—It must be stated that the gelatin solutions available to us for this investigation were quite viscous, especially if they were cool. For this reason, it is unlikely that 6 per cent gelatin solutions of the molecular size used by us could be used in cold climates, especially during military operations. However, to circumvent this difficulty, on a cold day, we have often diluted the gelatin solutions with equal parts of physiologic saline solutions. If such a mixture is kept at or about 35° C, no difficulty ensues in keeping the infusion running into the vein smoothly and readily.

(C) It can no longer be doubted that one of the greatest needs of a shocked patient is for a greater volume of circulating red blood cells. Therefore, gelatin solutions (as well as plasma) are at a disadvantage when compared to whole blood. For this reason alone, we would emphasize that in the rational management of patients in shock from trauma or burns, gelatin and plasma solutions should be reserved for purely *emergency* use. They can never be considered as true substitutes for whole blood.

SUMMARY

"Lightly and heavily" degraded gelatin solutions have been employed as a substitute for plasma in the treatment of shock caused by trauma or severe burns (Trauma—67 patients, burns—28 patients). Lightly degraded gelatin solutions seem to be retained longer in the blood stream, and appear to be as effective and safe as plasma in the management of these types of clinical shock.

We are indebted to our chief, Dr I. A. Bigger, who arranged the facilities that made possible these clinical shock studies.

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DISCUSSION—DR ALFRED BLALOCK, Baltimore, Md There is little I can add to what Doctor Evans has said, and I arise merely to express my thanks for what he has done in connection with the work of the Subcommittee on Shock He has been working closely with this committee during the past four years, and he has had, with Doctor Bigger's aid, one of the two best clinical programs on shock in this country The other has been that of Doctor Dickinson Richards and his group, in New York I have never known a young surgeon who was a more careful clinical observer than is Doctor Evans So many of us are prone to take to the laboratory problems which could better be studied on man, and Doctor Evans has shown an unusual ability to solve such problems

DR HUGH H TROUT, Roanoke, Va I hesitate to discuss Doctor Evans' paper, because I know nothing about the present use of gelatin As many of you recall, in World War I Hogan's gelatin solution was advocated In one of the hospitals with which I was connected, we had four deaths following the intravenous use of this solution

The autopsies in all these cases were done by the late Dr Hans Zinsser Doctor Zinsser was interested in these deaths because the solution came from his laboratory at Dijon In all four cases, the solution had been warmed preparatory to giving it intravenously to the patients Then something had happened to the patient for whom it was intended, Hogan's solution was then allowed to cool, and it was rewarmed and injected into the four patients that died

All four of these autopsies showed multiple pulmonary emboli of glycerin As a result of this experience, there was no further use made of Hogan's solution during the last war Doubtless Doctor Evans knows about this experience with Hogan's solution, and I would like to hear from him as to what became of this work

DR EVRETT I EVANS, Richmond, Va (closing) First, as to the problem of using a proper gelatin and getting it now, that cannot be answered The solutions that Dickinson Richards and I have been working with have been prepared under the personal supervision of an extremely competent chemist, who works 36 hours constantly while runs are being made, to assure us that the material is stable At present, enough is not being made for widespread use However, it is likely that in the next few months, after the Food and Drug Committee has gone over this material, we will be able to procure more The cost of plasma is running high, somebody has to pay for it The ward patient is charged nothing for it, but it costs somebody about \$20 I am sure gelatin will be sold for about \$1.50 to \$3.00 for 500 cc The Knox people will not put it out until we can be sure it is safe

About the matter of Hogan's solution We are not sure always from which gelatin source it was derived It can be made from animal skin or bone, or many types of animal tissue That made in 1918 was not a good solution for intravenous use, and it is likely that Doctor Hogan's solution was gelatin we would be afraid now to use You must never forget that gelatin, plasma and other materials are not true substitutes for whole blood, and the Sub-Committee on Shock should not be pointed out as remiss for not knowing this, it has been known for at least two years We must think of these as useful for emergency use, to be followed by whole blood, often in very large amounts

I am grateful for the remarks of Doctor Blalock, and I can say that it has been tremendously interesting to carry on in a clinical manner what Doctor Blalock has kept going from the last war to this Without his work I am sure we would have started at a place far behind what he has given to us by his beautifully conducted animal experiments

PENTOTHAL—METRAZOL ANTAGONISM*

A, METHOD OF SHORTENING THE RECOVERY PERIOD FOLLOWING
PENTOTHAL ANESTHESIA

A CLINICAL AND EXPERIMENTAL STUDY

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ALTHOUGH the ideal anesthetic agent for all major surgery has not yet been found, much progress has been made in anesthesia and the development of anesthetic drugs during the past decade. Among these advances are those associated with intravenous anesthesia, which has appealed not only to the experienced anesthetist, but to the surgeon and to the laity as well. When skillfully used, intravenous anesthesia displays advantages which make it the method of choice in many instances.

The first record of general anesthesia produced by the intravenous administration of a drug was reported in 1872 by Ore,¹ who used chloral hydrate. In subsequent years hedonal-chloroform, chloroform, ether, paraldehyde and alcohol were, likewise, employed in this way. More recently the newer drugs, sodium amytal, nembutal (pentobarbital sodium) and evipal, have found favor. To Lundy goes the credit for first using sodium pentothal (thionembutal). Since his first reports^{2, 3, 4, 5} on the use of sodium pentothal for intravenous anesthesia, more than 600 related articles have appeared in the literature.

Initially, the short-acting barbiturates or the intravenous anesthetic agents having a transient effect were advocated only for short operations. However, the "technic of intermittent administration" introduced by Lundy⁶ has permitted their application to longer operations. Sodium pentothal possesses many advantages recommending its use for prolonged surgical anesthesia. To the patient it is a nonirritating, odorless material inducing sleep rapidly and pleasantly and permitting comfortable recovery. For the surgeon it provides effective muscular relaxation without excessive capillary bleeding and, destroyed rapidly, it causes a minimum of functional and no organic injury during or after administration. In addition, it is inexpensive and can be stored without risk of chemical change.

While the advantages of intravenous pentothal anesthesia are many and varied, and certainly far outweigh the disadvantages, nevertheless, two faults

*Read before the Fifty-sixth Annual Session, Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

are recognized. The first is the apparent increase in the depth of anesthesia or narcosis which occurs at the termination of the operation when stimulation is no longer present and which is followed by a *prolonged period of sleep*. This postoperative period of sleep in some instances may last as long as eight or twelve hours, being, in general, proportional to the amount of sodium pentothal administered. While in some patients the prolonged period of postoperative unconsciousness is beneficial, in others it may be harmful. Pickrell has demonstrated that in experimental animals anesthetized with ether, avertin,⁷ or pentothal⁸ or in profound narcosis produced by the ingestion of ethyl alcohol,⁹ resistance to bacteria is lowered. Bacteria aspirated into the respiratory tract under these conditions grow uninhibited during the period of unconsciousness. The lessened resistance appears to be related to profound inhibition of the vascular inflammatory response, in the absence of which leukocytic emigration does not occur. Bacteria growing unrestrictedly under these conditions for several hours may become overwhelmingly numerous. If bacterial growth is unchecked, septicemia may ensue and death occur.

The second disadvantage in the use of sodium pentothal given intravenously is the possible occurrence of a state of *profound respiratory depression* which may be seen during any stage of the anesthesia. For the most part, the larger the amount of pentothal given, the greater is the tendency toward development of this condition. In some instances the state of depression may terminate in complete respiratory failure and death.

While untoward effects of pentothal are seen relatively infrequently, it is imperative to seek a means for averting the difficulties associated with respiratory failure and for alleviating the probably harmful condition consequent to prolonged narcosis. The latter is of especial importance in the instance of aged patients. Pentothal, in common with the other barbiturates, exerts a depressant action on the cerebrospinal axis and produces an effect varying from slight sedation to deep coma. In large doses the barbiturates depress directly the medullary respiratory center and both the depth and rate of breathing are decreased and irregular. To counteract these effects, several drugs have been employed. Those in common use are the respiratory stimulants coramine, caffeine, and picrotoxin. Another potent stimulant of this class, known for the past two decades, is metrazol. Synthesized in 1923,¹⁰ metrazol is classified pharmacologically as a central convulsant drug, similar in this respect to picrotoxin.

Metrazol was early found to possess a potent action antagonistic to the effects of various narcotics. Schoen¹¹ studied the arousing influence of the drug in narcosis induced by urethane, alcohol and paraldehyde. Extending the studies, Tartler¹² demonstrated a like effect of metrazol in narcosis caused by sodium barbital, and Barlow¹³ encountered the same finding in his extensive experiments with pentobarbital. In all of these experiments with barbiturate narcosis in animals, the mouse, rat, rabbit and dog, it was regularly found that, while its effects varied somewhat with the species, metrazol not only exerted a strong action to arouse the organism in narcosis, but, under

proper conditions of dose and time and route of administration, protected completely against lethal doses of barbiturates

Though these pharmacologic qualities of metrazol have long been established, few reports have been made of its action in pentothal narcosis in either animals or man. Piekenbrock and Olson¹⁴ used three cubic centimeters of metrazol intravenously after pentothal anesthesia and found the drug to be "a most efficient denarcotizing agent, and by its use the anesthetic state will be terminated promptly and any undesirable depression avoided." Reynolds¹⁵ considered metrazol to be a more effective analeptic agent than coramine, alpha-lobelin, or picrotoxin in arousing cats or dogs anesthetized with pentothal.

The possible value of metrazol in the prevention of prolonged pentothal narcosis and for the resuscitation of patients in profound respiratory depression was recently strongly impressed on the authors as the result of its effects in the treatment of a case to be described in a subsequent section. This experience has suggested further investigations of the drug in this respect. Clinical studies have been made of the arousing action of metrazol in patients anesthetized with pentothal and of its restorative action in respiratory and circulatory failure. These studies were supplemented by an examination of the effects of the drug in pentothal narcosis in rabbits and dogs. The results observed are described in the present report.

CLINICAL STUDIES

As noted above, the possible value of metrazol in counteracting the undesirable actions of pentothal was brought to the attention of the authors by difficulties experienced with a patient anesthetized with the drug.

The patient was a woman, age 24, who, several years before, had received extensive burns about the axilla. Subsequently, contractures developed between the trunk and the upper arm. Approximately 30 minutes after the beginning of an operation for the repair of the deformity, the patient's respirations suddenly ceased. There was no obstruction of the air passages, and the pulse rate and blood pressure had been normal. A total of 0.6 Gm of sodium pentothal in 2.5 per cent solution had been given. Artificial respiration was started immediately. Coramine, picrotoxin and caffeine in appropriate amounts were administered in rapid succession, but without evident effect. Death seemed imminent. The patient was cyanotic, and the pulse was barely perceptible. Five cubic centimeters of metrazol* were then administered intravenously, and almost immediately respirations were resumed, the pulse became full and strong, and consciousness was soon regained. Shortly, sodium pentothal was again rather cautiously administered, and the operation was completed within an hour. While the patient was still on the operating table, an additional three cubic centimeters of metrazol

* The metrazol used throughout the present work was the 10 per cent aqueous solution supplied commercially by Bilhuber-Knoll Corp., Orange, New Jersey.

were administered intravenously. The patient quickly recovered consciousness and expressed a desire to learn the results of the operation.

In this case it appeared likely that life was preserved chiefly by the action of metrazol, though the coramine, caffeine and picrotoxin administered may have exerted some influence on the result. The reviving action of metrazol at the depth of respiratory depression and the subsequent arousing effect at the termination of the operation were so striking that further clinical observations were undertaken.

The investigations with patients consisted essentially in the study of the effects of metrazol on the length of the recovery period after pentothal anesthesia. A series of observations was made first on the *average length of the recovery period* of 80 patients anesthetized with pentothal in the usual way, without subsequent administration of stimulants. In a second series of patients, more than 300, studies were made of the arousing effect of metrazol given intravenously at or near the close of the operative procedure. Pre-operatively, each patient received an hypodermic injection of 0.6 mg atropin and 10 to 12 mg morphine.

The procedure of anesthetization with pentothal was carried out in accordance with the "technic of intermittent administration" (Lundy,⁶ Cameron¹⁰ and Davison and Ruddle¹⁷). Pentothal in a 2.5 per cent solution was slowly administered intravenously, in combination with a mixture of 5 per cent glucose in 0.85 per cent saline. The dextrose was included, since Sise¹⁸ has shown that when the liver is well supplied with glycogen and when there is no lack of oxygen, liver damage does not occur. Richards has demonstrated that the use of the intermittent method allows one increment of pentothal to be partly detoxified before the next is administered.¹⁹ Pentothal is given only to adults, and the maximum dose does not exceed 2 Gm (80 cc of a 2.5 per cent solution). Lundy²⁰ has demonstrated that the incidence of phlebitis in the vein receiving the solution is directly proportional to the concentration of the drug. The importance of a continuous supply of oxygen as a supplement has been stressed by many writers, notably Lundy and Adams,²¹ Lahey,²² and Ravdin.²³ Most investigators believe that anoxemia is the basis of many anesthetic difficulties for it has been demonstrated that the barbiturates as a class affect the respiration by decreasing its depth. For this reason, the continuous administration of oxygen in high concentration is maintained during the entire anesthetic period.

The patients studied for the determination of the length of recovery period when no metrazol was given were carefully observed from the beginning of the anesthesia through the operation, and postoperatively until the patient could be readily aroused. As was to be expected, so many variables were found that it was difficult to determine an average recovery time. The amount of pentothal given, the weight and stature of the individual, the site and the extent or magnitude of the operation all affected the time of recovery. With the continuous stimulation and pain from the incision following operations upon the chest or the abdomen where the part could not be completely

immobilized, the recovery period was relatively short. In such cases in which the patients weighed less than 176 pounds (80 Kg) and received 1.5 Gm, or less, of sodium pentothal, the average recovery period was 1.5 hours. In instances in which the operative site was the extremities, scalp or face, where immobilization could be effected, the recovery period was definitely longer. The average period for such patients given 1.5 Gm or less of sodium pentothal was three hours with variations of 30 minutes to six hours.

In the group of 80 patients, there were 30 individuals weighing more than 176 pounds (80 Kg) but less than 190 pounds (86 Kg). The amount of pentothal given did not exceed 2 Gm, and in no instance did the operation last for more than two hours. The average recovery period for these patients with well immobilized operative sites was 3.5 hours. In the instances of those with poorly immobilized operative wounds, the period was two hours. While these values represent the average, in four patients the period exceeded six hours, in three patients, eight hours, and in two patients, 12 hours.

The Influence of Metrazol on the Length of the Recovery Period—The patients arranged in this category of the studies were given pentothal in the same way and in the same amounts as those not treated with metrazol. At the conclusion of the operation and the application of dressings, five cubic centimeters of metrazol were administered very slowly through the needle used for the introduction of the pentothal and the glucose-saline solution. In some instances, an additional quantity of three cubic centimeters of metrazol was given. The total dose was never more than eight cubic centimeters.

In all except 16 instances of more than 300, recovery took place either immediately or within 30 to 45 minutes after the patient was returned to the ward. In the 16 cases, in all of which the maximum dose of 2 Gm of pentothal had been given, recovery took place within 1.5 hours after the intravenous injection of metrazol.

The Restorative Effect of Metrazol in Respiratory Depression—Profound respiratory depression was seen and treated in six instances in addition to the case cited above.

CASE REPORTS

Case 1—Male, age 25. In preparation for radical dissection of the neck, intubation was undertaken. The patient's pharynx had not been treated with local anesthetic and difficulties were encountered in the intubation process because of lightness of anesthesia. In order to attain the desired depth of anesthesia, the dose of pentothal was increased. When 0.8 Gm had been given, the respiratory movements ceased. There was no visible obstruction of the air passages. The patient was given immediately 5 cc of metrazol intravenously. Without the aid of artificial respiration, active respiratory movements were established within 30 to 45 seconds and consciousness was restored within two minutes.

Case 2—Male, age 48. The conditions leading to respiratory failure in this patient were essentially identical with those of Case 1. Respirations ceased when the amount of pentothal administered was 1 Gm. Metrazol was given in 5 cc volume and recovery occurred as in Case 1.

Case 3—Male, age 45. This patient had been given 100 mg of novocaine intraspinally as the primary anesthetic agent for lumbar sympathectomy. About 15 minutes

later, during the course of the operation, the patient experienced severe pain in the operative wound. He was then given 0.8 Gm of sodium pentothal rather rapidly. Several minutes later, respiratory movements ceased, the blood pressure fell, and the pulse became imperceptible. He was given 5 cc metrazol intravenously. Irregular respiratory movements began almost immediately and the pulse could be felt. After three or four minutes, an additional 3 cc of metrazol were given intravenously. The respiratory movements resumed a regular rate, rhythm and depth, and, in addition, consciousness was almost fully restored.

Case 4—Female, age 38. When this patient had received a total of 1.6 Gm of pentothal, within 15 hours after the start of a radical mastectomy, her respirations ceased. Five cubic centimeters of metrazol were given and normal respiratory movements had begun at the termination of the injection. This dose of metrazol did not restore consciousness. No additional pentothal was necessary for completion of the operation, which was finished 30 minutes later. Three cubic centimeters of metrazol were then administered, and consciousness returned before the patient was removed from the operating room.

Case 5—Female, age 19. During the preparation of an abdominal tube-flap, 45 minutes after the onset of complete anesthesia, the patient had received 1.2 Gm of sodium pentothal. At this time the respirations became irregular and weak, although they did not cease. After the administration of 3 cc of metrazol, normal respiratory movements were resumed. The patient remained asleep and operation was continued.

Case 6—Male, age 56. This patient showed the presence of extensive granulating surfaces of the legs resulting from burns. After the operation for skin grafting had been in progress 80 minutes, at which time the grafts were being sutured to the granulating surface, the patient's respirations became irregular, shallow and then stopped. He had received 1.8 Gm of pentothal. The blood pressure and the pulse volume and rate were essentially normal. Artificial respiration was tried for at least three minutes, but was ineffective in stimulating voluntary breathing. Metrazol, 5 cc, was then administered intravenously, and within less than 30 seconds, irregular respirations began. Within three to four minutes the respiratory movements were full and normal. There was some movement of the lower extremities. Consciousness was not regained at this time. The operation was completed within 30 minutes, during which the patient received 0.2 Gm more of pentothal. At the termination of the operation and after application of the dressings, an additional 3 cc of metrazol were administered. The patient rapidly regained consciousness.

In these patients, no untoward reactions or ill effects have been noted, nor have convulsions occurred. There have been no instances in which postoperative fever or tachycardia could be attributed to the metrazol. No evidence has been seen of sensitivity or of localized reactions at the site of the intravenous injection. There have been no generalized phenomena, except the recovery of consciousness.

EXPERIMENTS WITH ANIMALS

Experiments were made in order to study the analeptic or restorative effect of metrazol in intravenous pentothal anesthesia in rabbits and dogs. For this 64 rabbits and 20 dogs were used.

EXPERIMENT I—The first study was concerned with the determination of the average recovery time following pentothal anesthesia in rabbits. For this, 16 rabbits were injected intravenously with 25 mg per Kg of pentothal in a 25 per cent solution. Measurements of time were made from the onset of unconsciousness until (a) the animal started to right itself with its head and front legs—the *righting period*, and (b) the animal could resume its normal position—the *recovery period*.

These periods, measured from the beginning of the anesthesia were (a) 27 minutes, with a variation of 15 to 43 minutes, and (b) 40 minutes, with a range of variation of 19 to 53 minutes

EXPERIMENT II—An attempt was made to interrupt completely and permanently the deep pentothal anesthesia in rabbits by the administration of metrazol. The same group of rabbits that had been used in the previous experiment, plus 16 additional rabbits, was employed. All were given 25 mg of pentothal per Kg in a 2.5 per cent solution into the ear vein. After 12 minutes, when the rabbits were deeply anesthetized, 100 mg per Kg of metrazol were administered intravenously. This resulted in an almost immediate "righting" of 30 of the 32 rabbits. Within two minutes after the metrazol injection, all animals had raised their heads and front legs, and the "recovery" of every individual was complete within ten minutes after injection of the metrazol.

EXPERIMENT III—For this experiment a more prolonged pentothal anesthesia was produced in 12 rabbits by the simultaneous injection of 20 mg of pentothal per Kg intravenously, and 35 mg per Kg of pentothal intraperitoneally. The average "recovery period" of the 12 animals was 48 minutes. The longest period of anesthesia was 70 minutes.

EXPERIMENT IV—The same group of animals employed in Experiment III and, in addition, 12 other rabbits were given 20 mg of pentothal per Kg intravenously, plus 35 mg of pentothal per Kg intraperitoneally. After 30 minutes, when each animal was deeply anesthetized, 50 mg of metrazol per Kg were given intravenously. In each instance, complete recovery had occurred within five minutes after injection of the metrazol. No convulsions were seen in any of the animals, although slight transitory twitchings were occasionally observed.

These experiments clearly demonstrate that it is possible to interrupt completely and permanently a profound pentothal anesthesia in rabbits by the intravenous administration of metrazol.

EXPERIMENT V—In this experiment studies were made on 12 dogs. Each animal was given 20 mg of sodium pentothal per Kg intravenously, and 20 mg per Kg intraperitoneally. The sleeping phase and the time for complete recovery, *i.e.*, when the dog could stand or walk, were noted. The average period for the group was three hours and 40 minutes. Several days later the same dogs were anesthetized in a like manner. After profound anesthesia had been continued for two hours, four dogs were given 35 mg per Kg of metrazol intravenously, four were given 30 mg per Kg, and four were given 25 mg per Kg. The dogs receiving the 35-mg-dose developed convulsions without shortening of the period of unconsciousness, and those receiving the 30-mg-dose developed subconvulsive twitchings without regaining consciousness immediately. The dogs that received the 25-mg-dose of metrazol developed transitory twitchings and were quite ataxic during the recovery phase.

EXPERIMENT VI—It was apparent from the results of Experiment V that immediate interruption of profound sleep in dogs due to pentothal was not possible through the administration of metrazol. It is well known that a considerable period of ataxia follows prolonged pentothal anesthesia in this species.

Therefore, in connection with the clinical purpose of the investigation, a further study was made of the possibility of shortening the *recovery time* after pentothal anesthesia in dogs, that is, the time for complete recovery after the first evidence of awakening.

For this purpose, eight dogs were given 20 mg of pentothal per Kg intravenously, and an equal amount at the same time intraperitoneally. Sleeping and recovery times as defined above were observed. Several days

later, the experiment was repeated and metrazol in doses of 20 to 37 mg per Kg were injected intravenously at the moment when the dogs began to awaken. As shown in Table I, there was a marked and constant reduction of the recovery time in every instance.

TABLE I

EFFECT OF METRAZOL GIVEN INTRAVENOUSLY UPON THE RECOVERY TIME OF DOGS ANESTHETIZED WITH SODIUM PENTOTHAL (20 mg /Kg Intravenously + 20 mg /Kg Intraperitoneally)

Dog No	Sleeping Time		Metrazol I V at End of Sleep*	Recovery Time		Remarks
	Hrs	Mins		Hrs	Mins	
69	1	45	None		30	
	1	36	35 mg /Kg		12	Transitory twitching slight ataxia walks
73	4	14	None	1	23	
	3	15	35 mg /Kg	1	1	Walks immediately slight ataxia
74	5	47	None	1	30	
	4	15	35 mg /Kg		3	Short attack of mild convulsions (fast injection) walks with some ataxia
75	5	00	None	1	50	
	5	25	20 mg /Kg		4	Walks slight ataxia
77	7	14	None		37	
	4	05	35 mg /Kg		15	Partly paravenous injection walks after 15 min
I	3	12	None	1	58	
	2	57	35 mg /Kg + 12 mg /Kg		9	Sits up after first dose walks after second
V	2	10	None	1	05	
	1	05	35 mg /Kg		2	Slight transitory trembling walks
Chow	4	27	26 mg /Kg		1	Walks immediately no ataxia

*The time at which the dogs started to raise their heads and made attempts to right themselves was taken as the end of the sleep.

DISCUSSION—Metrazol is a synthetic tetrazol compound, which is extremely stable and cannot be broken down or changed except by vigorous chemical procedures. It exerts a prompt and intense stimulating action on the vasomotor and respiratory centers in the medulla and on the cerebral cortex. This effect on the medullary centers is much more prominent when their functions are in a state of depression. When the circulation has been depressed by an hypnotic agent, metrazol causes a marked rise in blood pressure. It is relatively nontoxic insofar as the amount necessary to produce serious poisoning is concerned.²⁴ Its action is practically instantaneous when the drug is administered intravenously. It is absorbed very rapidly also when given by subcutaneous injection or by mouth. This is partly due to its extreme solubility in water. Its effects usually last 0.5 to 1.5 hours. It is rapidly detoxified, and its effects are not cumulative.

Pentothal, in common with all of the barbiturates, exerts a depressant action on the cerebrospinal axis. The depressant action may be employed in varying degree to induce calmness or sleep, to depress the motor cortex for the prevention of convulsions, and to produce partial or complete surgical anesthesia. In large doses the barbiturates act directly to depress the circulatory or respiratory center, especially the latter. In respiratory depression both the rate and depth of breathing are decreased, and the rhythm may be irregular. The barbiturates, even when used intravenously for

anesthesia, are not directly toxic to the myocardium, nor do they seriously alter the cardiac rhythm or conduction. A fall in blood pressure may result from the rapid intravenous injection of a relatively safe dose of a barbiturate, but the hypotension is transitory if the dose is not too large. Ectopic beats have been explained as the effect of transitory anoxemia and vanish when oxygen is given.

Consideration of the properties of metrazol and of the barbiturates in general reveals at once their essentially opposite pharmacologic effects. The expectation of possible antagonistic behavior when metrazol and the barbiturates are introduced into the same organism has been borne out in numerous investigations with animals. Tartler,¹² in 1929, showed that narcosis produced in the rat by sodium barbital in doses of 20 mg per 100 Gm of body weight was completely overcome by half the normal convulsant dose of metrazol, 2 mg per 100 Gm of body weight. Doses of 3 mg of metrazol, or more, resulted in permanent awakening. Conversely, Mehl²⁵ found that sodium barbital in quantities of 20 mg per 100 Gm of body weight protected rats against lethal doses of metrazol. These findings have been corroborated by many authors. As might be expected, the ultimate effect of metrazol is greatly dependent on the time of administration with respect to the introduction of barbiturates. The antagonism of the action of metrazol to that of sodium barbital in mice was established by Zipf, and his coworkers.²⁶

Somewhat similar antagonisms between barbital and metrazol have been observed in rabbits and dogs. Bailow¹³ found that narcosis in rabbits caused by 40 mg per Kg of pentobarbital was greatly shortened by metrazol and lethal doses were overcome. Rabbits given large doses of sodium barbital, 150 to 200 mg per Kg, were aroused immediately by intravenous injection of 25 mg per Kg of metrazol. The animals soon went back to sleep, however, and the state of consciousness was maintained only by the administration of repeated doses of metrazol. Koppanyi, Linegar and Dille²⁷ showed that metrazol given in divided doses would protect dogs against about three times the lethal dose of sodium barbital. Such animals did not awaken immediately but recovered ultimately.

Reports of studies on the antagonistic effect of metrazol in pentothal anesthesia have been limited. Reynolds¹⁵ injected dogs and cats with an amount of pentothal just sufficient to stop respiration. When artificial respiration did not initiate active respiratory movements, picrotoxin, coramine, alpha-lobelin, and metrazol were administered. Metrazol was found to be the most effective analeptic agent. Piekenbrock and Olson¹⁴ inject three cubic centimeters of metrazol intravenously following the termination of each pentothal anesthesia. These authors found it to be "a most efficient denarcotizing agent, and by its use the anesthetic state will be terminated promptly and any undesirable depression avoided."

The results obtained in the present work have shown that metrazol is an effective arousing agent in pentothal anesthesia in rabbits, a finding which parallels that of the previous investigations with sodium barbital and

pentobarbital in this animal. Under the conditions of the experiments, metrazol did not arouse dogs immediately from deep surgical anesthesia. In this respect, a species difference between rabbits and dogs is evident. However, it was clearly shown that the period of recovery of dogs, that is, the period from the beginning of awakening to complete recovery, could be markedly shortened by the action of metrazol. This result is in partial disagreement with that of Mousel and Essex,²⁸ who found metrazol and other analeptics of no value in treating severe depression caused by pentothal in experimental animals. The doses of metrazol used by these investigators were too low to permit final judgment on its usefulness. Furthermore, the present study has chiefly another object, namely, investigation of the possibility of shortening the recovery period after prolonged, but otherwise normal, pentothal anesthesia.

The findings in man, both from the point of view of the arousing effect of metrazol in surgical anesthesia with pentothal and its action to stimulate resumption of respiration in acute depression were most striking and, on occasion, dramatic. In this series of observations, the response of man anesthetized with pentothal appeared both quantitatively and qualitatively similar to that of rats and rabbits under the influence of sodium barbital and pentobarbital. While it was not possible completely to control the clinical studies, it was evident that metrazol was effective in markedly shortening the recovery period after surgical anesthesia and in arousing or protecting patients profoundly depressed by pentothal.

It should be emphasized that the use of metrazol is not recommended as a routine procedure but only in those cases in which indications for it are evident. In instances in which there is evidence of awakening at the termination of the operative procedure, the use of metrazol is not only unnecessary but may be harmful. With the wane of pentothal effect, there is a proportional increase in susceptibility to the convulsive action of metrazol. In the latter stages of pentothal effect, therefore, metrazol may induce convulsions.

It should be noted, further, that the pharyngeal reflex is not greatly diminished by sodium pentothal. For this reason, when intubation, bronchoscopy, or operations upon the throat are to be performed, the throat should be sprayed beforehand with a local anesthetic agent, such as pontocaine or cocaine.

SUMMARY

Studies were made on the antagonistic effect of metrazol in patients under sodium pentothal anesthesia. In control studies in which no metrazol was given the recovery from pentothal anesthesia varied from 15 to 12 hours, depending upon the size of individual and the dose given, and upon the magnitude of the operation. Patients weighing less than 176 pounds (80 Kg.) and receiving 15 Gm. of sodium pentothal recovered consciousness in an average period of three hours, when immobilization of the operative wound could be effected. In instances in which the operative site could not be immobilized, the average recovery period was 15 hours. Larger patients,

those weighing 176 to 190 pounds (80 to 86 Kg) and who did not receive more than 2 Gm of pentothal in operations lasting no more than two hours, recovered in an average period of 3.5 hours where the operative site was well immobilized. A shorter recovery period, two hours, was observed in patients in whom the operative site could not be immobilized.

In a series of more than 300 patients given pentothal in the same amounts and manner as for the control group, 5 to 8 cc of metrazol were administered intravenously. The recovery period, except in 16 instances, was not more than 45 minutes. Frequently, recovery of consciousness occurred almost immediately. In the 16 patients, all of whom received the maximum dose of 2 Gm of pentothal, recovery was delayed for not more than 1.5 hours.

In seven patients recovery from profound respiratory depression was effected quickly and so completely that operation could be resumed with the administration of additional pentothal.

Studies were made also of the arousing action of metrazol in pentothal anesthesia of rabbits and dogs. Narcosis in rabbits comparable in depth to surgical anesthesia was interrupted within five minutes and recovery was complete in every individual within ten minutes after the injection of metrazol. Dogs given metrazol during the stage of profound anesthesia could not be awakened immediately, but when metrazol was given at the first indication of awakening, the subsequent period of recovery was markedly shortened.

CONCLUSIONS

The administration of metrazol given intravenously markedly shortens the recovery phase following sodium pentothal anesthesia in man. In addition, it has relieved profound respiratory depression which has occurred in seven instances in the present study.

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DISCUSSION—COL WALTER DLNF WISL, Baltimore, Md I think this important paper merits serious consideration and there should be wide dissemination of the information, which might well counteract the bad effects of pentothal I rise simply to add my word of warning about the danger of this splendid anesthetic which is certainly, as someone has said, heaven-sent for use under present circumstances, particularly in the Navy, and also of great value in the Army We have not had, I am glad to say, in my Service Command, as much difficulty as I have learned about in civilian hospitals

It came to my attention two or more years ago that there were quite a number of catastrophes in civilian hospitals, possibly because of the casual manner in which it was administered, it was considered a simple procedure, apparently The patients were not properly prepared, the choice of case was not well made, and there were some very disastrous results All one need do is to mention this in a group of surgeons and someone will say "I know of a catastrophe or near catastrophe"—and relate one or more

instances As an illustration, I was asked to investigate a situation in one of our schools I found in one civilian hospital two recent deaths, one a student, one a woman, and from the description of the death of the student I imagine he could have been saved had metrazol been used I think everything else was used The chief thing I would emphasize is that it is a dangerous drug to use It is a wonderful anesthetic, but it cannot be used by people who are not qualified, and it must be stressed that it cannot be used casually and with free-wheeling

DR E I EVANS, Richmond, Va Just a few words about our experiences with pentothal In shock patients, in trying to shorten the time of anesthetic recovery, we were not very successful with either metrazol or picrotoxin I think everyone who uses pentothal much should inform himself by reading Dr Carl Moyer's paper published about a year ago, which contained certain facts not well known I have seen anesthetists when they got into trouble, start doing things which his work shows will be of little value They ask "Shall I give CO₂?" He points out that this is one of the worst things to do Even high oxygen concentration seemingly does more harm than good at that time The chief thing, if you get into trouble and do not have metrazol handy, is to use artificial respiration by pressure on the lower border of the costal cage (That does not mean you can do the same by intermittent positive pressure) To that can be added painful stimuli, such as slapping the costal cage His contribution, on this is most important

MAJOR BARNIS WOODHALL, Washington, D C About two years ago we reported a series of 378 major neurosurgical procedures carried out under a combination of pentothal and oxygen anesthesia We were pleased with our results chiefly, it must be added, because this anesthesia lowers intracranial pressure However, there were three patients in this group who suffered severe respiratory depressions and we were quite worried about these individuals Those of you who were at Ashford General Hospital on Monday will recall that Captain Galvin reported another group in which this agent had been used also for long operative procedures On the other hand, the Surgeon-General's office has reported six times as many complications with pentothal anesthesia as with any other anesthetic agent Doctor Pickrell's contribution, therefore, will be of considerable value to the surgeon using pentothal The major complication we have encountered, even under what we considered proper conditions, has been laryngeal spasm

DR ALTON OCHSNFR, New Orleans, La It might be well to call attention to the fact that metrazol is also not without danger Those who have seen it used in shock therapy will appreciate that it is a drug that must be used cautiously

DR KENNETH L PICKRELL, Durham, N C (closing) In answer to Major Woodhall's question relative to stridor and laryngospasm, I believe it is safe to say that there is considerable evidence that pentothal does not induce relaxation of the laryngeal constrictors In the cases studied in the present work, respiratory and circulatory failure were observed in two patients in association with attempts to intubate prior to operation Though these patients were under deep anesthesia, laryngospasm was evident and intubation was not possible without additional pentothal It was clear that the amount of pentothal necessary for induction of laryngeal relaxation closely approached the lethal dose It is to be noted that the danger associated with laryngospasm, especially in cases in which intubation is necessary, can be partially obviated in the beginning by spraying the throat with a local anesthetic such as pontocaine or cocaine

In the use of metrazol it is hoped that, by shortening the postoperative period of unconsciousness or the prolonged period of sleep following pentothal anesthesia, morbidity and mortality rates will be lowered This can be accomplished by decreasing the instances of postoperative pneumonia due to aspiration and hypostatic pneumonia, especially in patients of advanced years Further, through the initiation of early movement, vascular stasis and the formation of thrombi will be prevented A great advantage of metrazol is that, in addition, its action promptly and effectively relieves the profound respiratory depression which may occur during any stage of pentothal anesthesia

It is planned to continue these studies with nitrous oxide, ether, avertin and profound alcoholic intoxication It is possible that metrazol may be of comparable value in decreasing untoward effects of these materials as well

HEPARIN IN THE ABDOMEN*

A CLINICAL REPORT

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SINCE THE REPORT of Lehman and Boys¹ on the intra-abdominal use of heparin to prevent peritoneal adhesions there have been no other reports except by the same authors. For this reason it is necessary to present a brief review of their work, clinical applications, and conclusions.

It had been known for many years that fibrin was the corner-stone in the building of adhesions and that the organization of fibrin was the adhesion. Consequently, if the formation of fibrin could be prevented, it might be possible to keep adhesions from forming. As citrate, oxalate, and hirudin had been tried unsuccessfully, heparin seemed to be a logical weapon with which to attack the problem.

Lehman and Boys produced peritoneal adhesions in dogs by infection (opening and leaving open the appendix) and by trauma² (scarification of surfaces and gauze pledgelets sutured between ileum and cecum). The first method was later abandoned because of the mortality (50 per cent) in the animals. The animals were examined after six weeks and all of the intra-abdominal adhesions noted and separated chiefly by sharp dissection. Careful hemostasis was carried out by fine silk ties and electrocoagulation. Some of these animals were used as controls. In others, various substances were placed in the abdomen at the time of the separation of the adhesions and subsequently by paracentesis. All of the animals were again examined after two to six weeks.⁵ In those where no drug had been used in the abdomen the adhesions had reformed about 130 per cent. Where other substances, normal saline, amniotic fluid (amfetin), and papain were used, the reformation occurred greater than 100 per cent. Only when heparin was used was there a reduction in the number and extent of the adhesions. The percentages were estimated roughly by the number of adhesions cut. Later the width of reformed adhesions was found to parallel their number. When heparin was used the reformed adhesions were found to be about 34 per cent.

These investigators found that the best results were obtained by administering the heparin at the close of the operation and by paracentesis every 12 hours for three days. From these studies they worked out the technic detailed below for clinical use.

The following year they³ reported the use of the method on 14 patients, seven from their own, and seven from three other clinics. Their results

* Read before the Fifty-sixth Annual Session, Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

have encouraged us to try this procedure on a few (seven) of those obstinate people who seem to reform those adhesions which produce intestinal obstruction. Some people seem to have a tendency to produce adhesions in number and density far above the average. Whether this is due to a "fibroplastic diathesis" or from surgical defects resulting in chronic infection, as Boys¹ suggests, is still unknown. This group represents a serious problem to the surgeon. Many of them have to be, and are, operated upon repeatedly for acute intestinal obstruction. As Hertzler⁴ says "This sequence lasts as long as the patient does, or the hopeful persistence of the surgeon endures." In this class of patients heparin may be the answer and it may not. It seems to offer a better outlook than anything used up to now.

From our experience we agree with the original investigators that "Until greater experience has been had in clinical application, the use of heparin should be limited to cases of acute partial or complete intestinal obstruction due to adhesions and particularly to cases in which previous operations have been performed for obstruction or repeated threatening attacks. In other words, heparin should be used only in that group of desperate cases in which one is willing to accept the hazard of an insufficiently tried method in preference to a future risk of significant proportions."

"The one important and essential contraindication is the presence of an oozing peritoneum after adhesions have been divided. Heparin should not be used when granulations or subacute inflammatory tissue is present whether hemostasis seems complete or not."

To this we would add that the time following an abdominal operation, when with safety the abdomen may be reopened, adhesions separated, and heparin used, should not be less than two months. Furthermore, we would not use heparin in the abdomen in those patients where the obstruction was due to a single band of adhesions even though the patient had had repeated episodes of obstruction.

We do not think accidental opening of the bowel during the dissection is a contraindication, as this happened to several of our patients without untoward effect.

The technic of administration as used by Lehman and Boys³ is as follows. After the operation for division of adhesions is completed a Pezzar catheter is introduced into the abdomen through a stab wound in the area nearest the maximum number of adhesions. The abdomen is closed and 10,000 units of heparin in 300 cc of normal saline solution is instilled through the catheter which is then clamped and the patient returned to bed.

Blood counts, coagulation time (by the capillary tube method), and blood pressure readings are taken every two hours for six hours, in addition to the usual readings of temperature, pulse and respiration. Coagula-

* Lehman and Boys used heparin from the Connaught Laboratories of the University of Toronto and liquaemin made by Hoffmann-LaRoche, Inc. We have used the Lederle preparation in 10 cc vials containing 1,000 units per cc.

tion time is longest two hours after heparin is given, when the concentration reaches its maximum in the blood. These readings are taken again just before the introduction of each dose of heparin. Every 12 hours after the operation a dose of 5,000 units in 300 cc normal saline is instilled through the catheter until 40,000 units have been administered during a period of three and one-half days. The catheter is withdrawn six hours after the last instillation.

They repeatedly assert the necessity for discontinuing the heparin and giving transfusions of whole blood should clinical or laboratory signs of bleeding occur, as the action of heparin is quickly neutralized by protamine of the blood.

In Lehman and Boys' series of 14 cases, they have had 11 smooth post-operative recoveries. One death they attribute to insufficient observation and failure to give transfusions. Autopsy showed this death was due to intra-abdominal hemorrhage of diffuse indeterminate origin. The maximum coagulation time was seven minutes. This patient was operated upon and adhesions separated, obstruction relieved, and heparin given just 15 days after resection of two feet of small bowel had been performed for the relief of obstruction due to volvulus. Apparently the volvulus was caused by adhesions formed at the time of a pelvic celiotomy four years previously. The authors believe the recent operation 15 days before should have contraindicated the use of heparin in this case. One patient had a rather severe toxic (?) reaction from doubtful heparin, one patient had symptoms suggesting hemorrhage, and one had slight wound bleeding. There were no cases of wound disruption, only one had slight pain during administration of the drug, and only one had slight ileus. One, Case 8, developed a pelvic abscess, requiring vaginal drainage, and infection of the abdominal wound. An analysis of their 14 cases is adapted in Table I from their report.

They point out in their conclusions that hemorrhage will always be a potential danger, that this danger can be circumvented by proper clinical and laboratory observations, and that no data have yet been presented to show the effectiveness of the method in preventing adhesions in the human being.

In our seven cases we have modified the technic of administering the heparin after the first operating room dose by giving 10,000 units every 12 hours until a total of 40,000 units has been given. Thus, the total is the same but it is delivered over a period of 36 hours instead of the three days and a half required when 5,000 units are given every 12 hours. We have done this because we have assumed that most of the peritoneal exudate was poured out during the first 24 hours after the operation. We have also carried out our usual treatment following abdominal operations and have given prostigmine 1 cc of a $\frac{1}{2000}$ solution subcutaneously every four hours for eight doses and then every six hours for eight doses accompanied by the insertion of a rectal tube for half an hour or longer at each injection.

HEPARIN IN THE ABDOMEN

TABLE I
Lehman and Boys

	Race	Sex	Age	Surgeon	Prev Laps	Prev Obs	Heparin Used	Technic	Max Cg Time	Post-Op Course	Complications	Last Seen Post-Op
1	C	M	44	L & B	0	0	Connaught	One dose 1,000 u		Ileus	0	8 days
2	C	M	34	L & B	2	1	Connaught	Standard	6 m	Smooth	0	4 mos
3	C	F	51	L & B	1	0	Connaught	Standard	7 m	Smooth	0	2 mos
4	W	M	53	L & B	1	1	Connaught	Standard	7 m	Smooth	Mild bron pneum	13 days
5	W	M	60	L & B	2	1	Connaught	Standard	5 m	Smooth	0	14 days
6	C	F	34	L & B	2	1	Connaught	20 000 u 3 doses	7 m	Died	Hemor-rhage	2 days
7	C	M	65	L & B	1	1	Connaught	15 000 u 2 doses	5 m	Smooth	Hemor-rhage?	14 days
8	W	F	40	Firor	Numerous	Sev-eral	Connaught	40 000 u 4 doses	Normal	Smooth	Slight wd hem	6 mos
9	W	F	45	Owings	4	2	Toxic brand	15 000 u 1 dose	3½ m	Severe toxic (?) react		6½ mos
10	W	F	60	Freed	11	Num	Connaught	Standard		Smooth	0	1 mo
11	W	F	Ad	Freed	1	?	Connaught	Standard		Smooth	0	
12	W	F	42	Horsley G	2	1	Connaught	10,000 u 1 dose		Smooth	0	21 days
13	W	F	46	Horsley J S	1	?	Connaught	30 000 u 5 doses		Smooth	Slight pain	
14	W	F	32	Horsley G	1	?	Liquaemin	15 000 u 3 doses		Smooth	0	

TABLE II

	Race	Sex	Age	Prev Laps	Prev Obs	Heparin Used	Technic	Max Ven Cg Time	Post Op Course	Complications	Last Seen Post-Op
1	W	F	44	1	Numerous	Lederle	40 000 u 4 doses 36 hours	22 m	Smooth	Mild wd bleeding	2½ years
2	W	M	54	2	2	Lederle	50 000 u 5 doses 48 hours	13 m	Stormy	Failure of healing Hernia	2 1-3 yrs
3	W	F	45	1	1	Lederle	40 000 u 4 doses 36 hours	8 m	Stormy	Ileus	11 mos after 2nd op Pain No obstruc
3	2nd op			2	2	Lederle	40 000 u 36 hours	10 m	Stormy	Wound infect	
4	W	F	25	3	2	Lederle	Same	7 m	Stormy	Hem III Pelvic abscess	1½ mos
5	W	F	33	1	3	Lederle	Same	40 m	Stormy	Hem II Abd wall abscess	1½ mos
6	W	F	36	2	2	Lederle	Same	8 m	Smooth	Slight ileus	4 mos
7	W	M	52	2	4	Lederle	Same	8 m	Stormy	Ileus	2 mos

CASE REPORTS

Case 1—Mrs E B, white, age 44, was admitted to St Joseph's Hospital, November 5, 1941, complaining of pain and cramping in abdomen. She had had the uterus and appendix removed in 1929, and had had repeated attacks, two or three times each month, of abdominal pain and cramping since, usually accompanied by nausea and vomiting. Except for chronic constipation she had been comfortable between attacks. There was moderate distention on admission. She was relieved by a Wangenstein tube, and left the hospital on November 14. She was advised to return for operation for release of adhesions. She was readmitted January 7, 1942, having had several "mild"

attacks in the interim. The blood count, pressure, and venous coagulation time were normal.

Operation—January 8, 1942. Many adhesions were separated, and in freeing the small bowel from dense adhesions in the right pelvis the lumen was accidentally opened. There was no gross soiling from this. After repair with "intestinal" catgut, the dissection was completed and heparin 10,000 units (Lederle) in 300 cc normal saline was introduced by the method of Lehman and Boys. Thereafter 10,000 units was introduced every 12 hours for three doses—total 40,000 units. There was slight abdominal distention but no nasal gastric tube was required. There was some bleeding from the incision and around the tube, but the blood count remained above 4,000,000 and the hemoglobin above 75 per cent. The maximum pulse rate was 110, the systolic pressure was never below 120. The maximum venous coagulation time was 22 minutes. This occurred two hours after the second 10,000 units was given, i.e., 14 hours after operation. It returned to a normal six minutes four days after operation. She made a smooth convalescence and left the hospital January 24, 1942. She has been seen several times since, the last time in July, 1944. She has had no further attacks, and has been free from pain.

COMMENT. This case needs no comment except to call attention to the fact that opening the bowel during dissection did not lead to any unfavorable result in the presence of heparin. This was predicted by Lehman and Boys¹ on the basis of their experimental work.

Case 2—E. P., white, male, age 54, was admitted to St. Joseph's Hospital, March 8, 1942, with abdominal pain, cramping, vomiting, and distention of 24 hours' duration. He had had his appendix removed in 1932 and, in 1936, had had an operation for acute intestinal obstruction. Adhesions were separated but no bowel was removed. He had been well until two days before the present admission. He was relieved by enemata and was feeling well on the third day. Roentgenologic study of the colon showed no abnormality and he was dismissed one week after this admission. He was readmitted, April 2, 1942, with obstruction of less than 24 hours' duration. This was, again, relieved by enemata and, at his request, operation was performed.

Operation—April 4, 1942. The adhesions were so widespread throughout the right lower abdomen and in the pelvis that an hour was required to free the small bowel everywhere from surrounding structures and from other loops of small bowel. No attempt was made to separate adhesions between the cecum and abdominal wall. Because of the extent of the adhesions this man was given 10,000 units of heparin every 12 hours until 50,000 units were given. He had moderate distention, looked sick, and a Wangenstein negative pressure gastric tube was kept in place for four days. His pressure, pulse rate, and temperature remained within normal limits. His abdominal dressings were saturated with serosanguineous drainage but there was no free bleeding. His maximum venous coagulation time was 13 minutes two hours after operation but did not exceed seven minutes thereafter. On the eighth postoperative day the wound looked good, the sutures were removed, and immediately the wound separated down to the peritoneum which remained intact. There was no gross evidence of infection in the wound. The abdomen was strapped firmly and the wound healed slowly by second intention. He was dismissed May 3, 1942. He returned for repair of a large incisional hernia on December 3, 1942, and we had the opportunity of exploring his abdomen. No adhesions could be found except those between the cecum and anterior abdominal wall which had not been cut at the time of his heparinization. He was repaired with interrupted sutures of cotton. This time he did well until he developed a slight cough and his hernia recurred through the upper half of the incision. As the skin was holding well it was thought best not to repair the rupture again at this time. This was

done successfully June 12, 1943. He was seen last without symptoms and without hernia in August, 1944.

COMMENT This patient is interesting because his is the first case we know of where there has been an opportunity to study effect of heparin on the reformation of adhesions in the human abdomen. It is quite possible that the large amount of heparin, 50,000 units, was the causative factor in the failure of his wound to heal.

Case 3—Mrs. H. A., white, age 45, was admitted to the Good Samaritan Hospital, April 8, 1942, complaining of repeated attacks of pain in the abdomen. These were sometimes accompanied by nausea and vomiting, were always cramp-like, and ordinarily lasted for only a few hours. She had had typhoid fever with peritonitis (perforation?) at the age of nine. There had been vague abdominal pain for many years but no severe attack until 1936. She had been married 21 years but never pregnant. In 1937, she had been operated upon for intestinal obstruction, but adhesions were found so universal and dense that nothing much was done. Between this and the present admission, there were several episodes of intestinal obstruction, but our operation on April 14, 1942, was performed when obstruction was not present.

Operation—The small bowel, densely adherent to the anterior abdominal wall, was accidentally opened at the beginning of the operation. After working for two hours, the right lower quadrant was cleared by sharp dissection and the usual heparin treatment was begun until she had received 40,000 units in 36 hours. She had a stormy course and there was considerable distention. There was thin blood-stained drainage from the incision and around the catheter but no evidence of significant hemorrhage. The maximum coagulation time was eight minutes. She was dismissed on the 15th day after the operation.

She was greatly improved, though she had some pain, until another attack of obstruction occurred in August, 1943. We undertook our second operation September 29, 1943, again, when no obstruction was present.

Operation—September 29, 1943. This time, because the recent pain had been in the upper abdomen, we made a high right rectus incision. Universal dense adhesions were encountered. The liver was fused with the subphrenic peritoneum. The intestine in the right lower abdomen, which had been released 17 months before, was free, mobile, and smooth, without adhesions. Again, the procedure lasted more than two hours and the small bowel was entered three times in the dissection. Heparin, 40,000 units, was given as before.

Her course was again stormy and an abscess in the lower half of the incision did not prove serious. The maximum coagulation time was seven minutes. She left the hospital on the 18th day. When last seen, months later, she was greatly improved, and though there had been some pain there had been no obstruction. She felt that "her operations had been worth while."

This was the second, and only other time, we have had the chance to see the effects of heparin on the reformation of peritoneal adhesions. The contrast between the previously "cleared area" and the thick jungle of adhesions elsewhere was striking.

Case 4—Mrs. L. H., white, age 25, was admitted to the Good Samaritan Hospital, September 13, 1942, having two days before recovered from pain in the abdomen, vomiting, and distention of 24 hours' duration. She had had an abdominal tumor removed

at the age of 13, an "acute appendix" removed in September, 1941, and an operation for acute intestinal obstruction in December, 1941

Operation—September 18, 1942 This was performed with the patient in good condition and no obstruction present The small bowel was adherent to the right broad ligament, where an ovary had been removed This was separated, leaving a raw area in its serosa three inches long Heparin was given, 40,000 units in 36 hours On the day following the operation she looked sick, there was moderate distention, temperature 101° F, pulse 116 The hemoglobin had fallen to 69 from 89 per cent before operation, the red cells from 4.4 million to 3.5 million The blood pressure did not fall below 110 The coagulation time was six minutes We felt that she was bleeding but that our margin of safety was still wide We continued the heparin treatment and withheld blood The temperature continued from 100° to 102° F, the hemoglobin and red cells continued to fall, but the blood pressure and general condition remained about the same and the abdominal distention was less On the third postoperative day, 36 hours after the last 10,000 units of heparin, the red cells were 3 million, the hemoglobin 42 per cent Daily transfusions of 300–500 cc of blood were given for the next four days She improved rapidly, though the daily temperature rose above 101° F

On the 15th postoperative day a pelvic abscess was drained through the posterior vaginal fornix Following this she made a good recovery The abdominal wound healed well and she left the hospital 26 days after the first operation She was well one month after leaving the hospital

COMMENT—In this case we assumed a big risk to keep from neutralizing the action of the heparin In this instance the result justified us, but so grave a chance will not be taken again

Case 5—Miss R F, white, female, age 33, was admitted to St Joseph's Hospital, December 18, 1942, with a story of four or five attacks of severe abdominal pain with vomiting, since a ruptured appendix had been removed in July, 1942 The last attack was two days before admission After six days, during which the obstruction we thought had been relieved by the Wangenstein tube, the cramping pain continued intermittently, so operation was performed

Operation—December 24, 1942 Several loops of small bowel were dissected from the pelvis, one completely obstructed but not strangulated Ten thousand units of heparin was instilled every 12 hours for four doses The patient was distended the following day, the coagulation time was 40 minutes and the hemoglobin had dropped to 69 per cent from the preoperative figure of 81 per cent She was given 400 cc of blood and the heparin treatment was continued She remained somewhat distended, the temperature ranged from 100° to 101° F, pulse maximum 120 The blood pressure was never below 115 There was the usual serosanguineous drainage from the wound Following the transfusion the coagulation time fell to 11 minutes and was never above 12 minutes during the heparin treatment It returned to six minutes two days after heparin was stopped On the 10th postoperative day the stab wound in the right lower abdomen looked angry It was opened and an ounce of pus obtained Two days later the incision showed an abscess which was similarly opened These places continued to drain and she gradually regained strength After three more blood transfusions she left the hospital February 13, 1943 She was last heard from six weeks later, and seemed to be entirely well

This case illustrates, again, the danger of hemorrhage and the possibility of wound infection

Case 6—Mrs J M, white, age 36, was admitted to the Good Samaritan Hospital May 4, 1944 Her appendix had been removed in 1939, and both tubes and left ovary

taken out in 1941. For three months prior to the present admission she had had cramping abdominal pain with nausea and vomiting. The last of these attacks was two weeks before the present admission and continued for eight or ten hours.

Operation—May 5, 1944. A single loop of ileum was released from the back of the uterus and right ovary, a posterior round ligament plication done to cover the raw area on the uterus. Forty thousand units of heparin was given in the usual manner. Her convalescence was smooth in every way. The maximum coagulation time was eight minutes. She was dismissed on the 16th day after the operation. In September, 1944, she was well and had had no further trouble.

This case was satisfactory, but the very limited extent of the adhesions did not justify the use of heparin.

Case 7—A white male, age 52, was admitted to the Good Samaritan Hospital with acute obstruction of four hours' duration. His appendix was removed in 1936. He began to have attacks of obstruction in 1937 and was operated upon for this in 1941. He does not know just what was done at this operation. Because his condition was good, the obstruction had been present less than six hours and distention was only beginning, we operated upon him as soon as he was admitted.

Operation—There were many adhesions between the ileum and anterior wall and several loops were involved. There was complete obstruction at one point due to one thick band around which the loop of bowel had become angulated. Forty thousand units of heparin were given in the usual manner. His course was uncomfortable, due to distention, there was the usual profuse thin bloody discharge around the tube and from the incision but no signs of hemorrhage. The maximum coagulation time was eight minutes. He left the hospital on the 15th day after the operation. When seen November 15, 1944, he was having no trouble.

COMMENT This was an ideal case for the use of heparin and, though he was quite uncomfortable for four days, his result so far has completely justified the treatment.

No worthy conclusions can be drawn from seven cases. The original investigators point out that there must be many hundreds of cases coming to autopsy or subsequent operation in which heparin has been used before a real knowledge of its usefulness can be obtained. While this may be true, we think that the clinical test is easier of fulfillment and more satisfactory practically. If it can be shown that large numbers of people with repeated attacks of, and operations for, intestinal obstruction, who have had no relief from surgery, have been set free by heparin, then we can afford to accept it without waiting for the operating room and necropsy to tell us. Until then the whole subject of its clinical application must remain *sub judice*.

It is quite likely that intravenous administration of the drug in much smaller quantity will be as effective as the intra-abdominal route—with less peritoneal reaction.

On account of the edema and congestion in the wall of an obstructed loop of bowel it is probably safer to limit the use of heparin to the interval between attacks of obstruction. We believe the drug should not be used when resection is undertaken, though accidental opening of the bowel as we have

definitely shown, is not a contraindication. The use of the drug should certainly be limited to those people who have had one or more episodes of obstruction, and it is in no sense a prophylactic reagent in routine abdominal surgery.

In our small series those patients who have been followed for more than a year, all of whom have had one or more attacks of obstruction, have been completely relieved.

CONCLUSIONS

1 Intra-abdominal heparin to prevent obstructing adhesions should be limited to those who have had one or more operations for obstruction or repeated attacks following abdominal surgery.

2 The hazards are hemorrhage, infection, and possibly delay in wound healing.

3 The contra-indications to its use are recent abdominal surgery, incomplete hemostasis, and possibly intestinal resection.

4 The hazards should be recognized promptly when they appear, and can be checked by blood transfusion.

5 Red cell and hemoglobin determinations, blood pressure reading, and the general appearance of the patient are better guides in postheparin treatment than any known coagulation time tests.

6 Accidental opening of the bowel during the dissection of adhesions is *not* a contraindication for heparin administration.

7 In our small series we have been pleased with the complete absence of obstruction in the months and years following the use of heparin in the abdomen.

8 Until there are more clinical reports we must consider the use of heparin to prevent "obstructing" adhesions as promising but unsettled.

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DISCUSSION—DR E. P. LEHMAN, University, Va. I have been greatly interested in this paper, as I have a considerable personal stake in the method. I like very much Doctor Massie's conservatism in stating the absence of definite conclusions to be drawn from the clinical material now available. The method has sufficient potential danger so that it must be limited to those cases of repeated operation for obstruction in which one is willing to run a risk for the sake of much needed relief.

Recently, at the University Hospital, we have seen no cases in which we felt the method to be justified, either because there had not been repeated obstructions, or because hemostasis was incomplete. I, therefore, have nothing to add from the clinical angle on the use of this procedure.

I was particularly interested in the two cases in which Doctor Massie demonstrated at a second operation the absence of adhesions in the area treated. I had rather hoped that a larger number of surgeons would interest themselves in this method, because

I have felt and still feel it has promise. The experimental results have been consistently conclusive. I hope we will hear more of it in the future, and thank Doctor Massie for keeping the subject alive.

DR WALLER O BULLOCK, Lexington, Ky. I had the opportunity to observe some of these cases of Doctor Massie's, and I was impressed with the gravity of the conditions they present. Usually a surgeon does not consider with a friendly eye disruption of wounds and postoperative hemorrhage, yet these complications were present in several of Doctor Massie's patients. However, the fact that he has shown that the adhesions have disappeared from the field of operation, make me satisfied that the method has some good, and when the bugs get worked out of it, as they say about machinery, it will prove a useful agency in such cases.

DR FRANCIS M MASSIE, Lexington, Ky. (closing) The drug is expensive, it costs about \$5.75 for 10,000 units, and that may limit its usefulness.

I do not know whether or not it is any good. I have used it in seven cases in three years in which I thought it was applicable. I think it is the most promising thing we have had.

I believe concentrating the drug in 36 hours instead of three and one-half days has increased the postoperative risk, but has tended to reduce the adhesions which have reformed.

METHODS OF CONSTRUCTING A VAGINA*

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AN UNUSUAL FEATURE of this report is that four different methods, determined by pertinent circumstances, were utilized to construct vaginas in four women in whom that organ was congenitally absent. Other surgeons have described their results in these cases, but in most instances, each surgeon has recommended only one form of treatment which he has used on all the women under his care. My experience would indicate that several different methods can, if properly used, be equally effective. The choice of methods should be based not only on the anatomic findings present, but also on the temperament, the marital status, the intelligence and cooperation of the woman one is treating.

In my fourth, or most recent case, the flap used to cover the posterior wall of the vagina was made in a way, which, so far as I can find out, has not been described previously, although probably the same technic has been employed by others. Except for this one operative step, there is nothing new in the methods of treatment used in my four cases.

No detailed description of the embryologic defects which result in a woman being born without a vagina will be presented. It will suffice to point out that all the women I treated showed the typical findings which are seen when the lower ends of the two müllerian ducts fail to develop. The only vestiges of a vagina were shallow depressions in the perineum not over 1-1.5 cm in depth. These represent merely the small terminal portion of the vagina which develops from the urogenital sinus in connection with the external genitalia and does not arise from the müllerian ducts. In my cases, in which the abdomen was opened, small uteri varying from 2-2.5 cm in length were found—not only in size, but in general development so immature as to make it impossible for them to function, no matter how much hormone therapy might be used. The ovaries, on the other hand, appeared normal. None of the four women showed any signs of hermaphroditism.

Before attempting to make a vagina, a surgeon will want to know the normal dimension of that organ. Most authorities stress the fact that the anterior wall is shorter than the posterior because the vagina is united to the uterus at an acute angle. According to Williams' textbook, the length of the anterior wall varies from 6 to 8 cm while that of the posterior from 7 to 10 cm. Curtis gives 6.5 cm as the length of the anterior wall, and 8 cm as that of the posterior. Wharton writes that the normal adult vagina is about 8 or 9 cm deep.

What is perhaps more important than the measurements of the normal

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vagina is what length and circumference are necessary for the completion of the sex act satisfactorily both for the woman and her husband. This will, of course, vary to some extent with the husband, but it is certain that in many instances a vagina considerably shorter than the normal length permits satisfactory marital relations. I recently examined a woman whose vagina measured only 5 cm in length, and she had never suffered from dyspareunia, and regularly experienced orgasm. Her husband, who is apparently a normal man, states that sexual relations are entirely satisfactory to him. The patient has never menstruated, and she has a very small uterus which does not connect with the vagina.

In March, 1935, I saw the first patient of this series. She was then 15 years old and had been married three months. Repeated attempts at sexual relations had been unsuccessful. She had never menstruated. The breasts were well developed. The pubic hair showed typical feminine distribution. On palpation, definite tenderness over McBurney's point on the right was elicited and the patient gave a history of having had several attacks of acute appendicitis. Inspection of the external genitalia showed a normal, but not an hypertrophied clitoris. The labia majora were normal. The labia minora were unusually long and pendulous—something that is occasionally seen in women who are otherwise normal. At the usual site for the vaginal orifice, there was a small opening which would just admit the tip of a Kelly clamp for a distance of only 1 cm. There was no cervix to be felt or seen in this depression. On rectal examination, a small uterus was felt. Normally developed ovaries were palpated.

Because of the repeated attacks of appendicitis, a celiotomy was performed. This gave us an opportunity to inspect the pelvic organs. The uterus was normal in contour, but only 2.5 cm in length. The fallopian tubes were rudimentary. The ovaries were normal, the right showing a moderately well developed graafian follicle. The appendix was removed, and the patient was then placed in the perineal position. A circular incision was made around the outer margin of the mucous membrane surrounding the perineal depression, following the line where the skin and mucous membrane meet. By blunt dissection, the tissue under the mucous membrane was spread apart. Then, in the same manner, the tissue laterally, anteriorly and posteriorly were all gradually stretched until finally there was a tunnel 7 cm in length and of sufficient diameter to admit two fingers. The small circular bit of mucous membrane which had originally covered the very immature vagina had been pushed further and further upward while this was being done, so that it finally rested on and covered the top of the newly made vagina. However, all the rest of this 7 cm long tube was raw and covered with neither mucous membrane nor skin.

Using a method similar to, but not exactly like, the method described by Graves, and later by Davis and Clon, the following attempt was made to cover over these raw areas. The labia minora were dissected off from above downward in such a way as to leave pedicles large enough to furnish good

circulation The available mucous membrane in each flap was increased by splitting apart from below the surfaces of each labium minus, thus, converting the large folds into flat surfaces These flaps were then sewed deeply into the vagina with No 0 chromic catgut The raw areas left by dissecting away the labia minora were then covered by sewing together the adjacent skin surfaces with interrupted sutures of plain catgut Care was taken, both in making these flaps and later in covering all the raw areas, not to injure in any way, or encroach too closely on, the clitoris

This patient was fortunate in having unusually long labia minora, for by using them, as just described, it was possible to cover over the entire lateral and most of the anterior and posterior walls of the newly constructed vagina Usually, all that can be done with the labia minora is to cover over the lower part of the lateral walls, as the small lips are seldom long enough to stretch beyond this, no matter how the pedicles are cut

At the time (1935) that this operation was performed, Wharton, not having reported his work with the artificial phallus made of balsa wood, I made one of plaster, covered it with a rubber condom, and inserted it into the artificially made vagina, where it was kept for the first ten days of the patient's convalescence After leaving the hospital, the patient used it every day for three months as a dilator It was then possible to introduce a full-size speculum into the vagina without causing her any discomfort

It was impossible to find out immediately after this operation, whether or not it was successful, for the patient, suspecting her husband of contracting gonorrhea while she was in the hospital, refused to permit sexual relations She obtained a divorce shortly after, stopped using any dilator, and left the city Two years later, she remained and wrote me that marital relations were entirely satisfactory She was having no dyspareunia and experienced orgasm One year later, while in Baltimore, she came to my office The vagina still easily admitted two fingers, was 7 cm in length, and permitted the introduction of a full-size speculum

In this case, the unusually long labia minora and the patient's youth were factors that doubtless helped in obtaining a good result It is worth emphasizing that even though the patient went two years after the operation without using any dilator, the vagina did not contract, as it so often does if dilatations are discontinued It measured 7 cm in length at the end of that time, and easily admitted two fingers

In the second case, an operation was refused This refusal came not from the patient, but from the man to whom she had been engaged for many years, and later married He would not consent to his fiancée being subjected to the risk of an operation no matter how slight the danger might be Knowing Frank's and also Holme's successes in making a vagina without an operation, I decided to try Frank's method

This patient, an unusually attractive woman, age 21, was referred to me by Dr Leshe Gay She was, at that time, a student nurse The general examination was negative The breasts were normally developed The labia

majora and the labia minora were normal. The urethra was normally developed. Between the urethra and the anus, there was not even a dimple to indicate where the vagina should be. On rectal examination, a mass about 2 cm in length was palpated which the examiner thought was probably the uterus. One ovary was definitely felt.

The patient was given a pyrex glass rod $\frac{5}{16}$ of an inch in diameter, and told to press with this rod on the perineum over an area midway between the urethra and anus. At first, pressure was directed mostly backward, so as to keep from injuring the urethra. The direction of the pressure was changed at the end of a few weeks to upward and backward, following the same axis that the normal vagina takes. This patient was very intelligent and conscientious. She worked with the pyrex tube for at least a half hour, two to three times a day, and reported to my office once or twice a week where I used the tube and my gloved finger, endeavoring to help in producing a vagina.

Progress was slow, but steady. At the end of six weeks, there was an opening which would admit the tip of a finger for a depth of 2 cm. When a little bleeding would occur, as it occasionally would as a result of trauma, the patient stopped treatments for 48 hours. Every night before going to bed, she applied to the perineum, an ointment containing estradiol. This may have been helpful. Certainly its use seemed logical. Six weeks later, the patient was able to introduce the glass rod 4 cm. She was then given a pyrex tube $\frac{5}{8}$ of an inch in diameter. Three months later, or about six months after treatment was started, three fingers could be introduced into the vagina which was now 6 cm long. The patient married, and has written me stating that sexual relations are entirely satisfactory to both her husband and herself, and has expressed gratitude for what was done for her. She has adopted two children and is very happy.

After reading Frank's article on the production of a vagina without operation, and of learning of Holmes' and my success with this procedure, one might ask why not use this method in all cases. Personally, I think it has marked limitations. This patient treated herself for six months, and the treatments were definitely painful. Only her conscientiousness in carrying them out made success possible. She was never able to wear any of the vaginal forms recommended by others. She tried them, but was unable to sleep with the form in place, and could not carry out her duties as a nurse while wearing one in the day time. When a patient has a small vagina to start with—perhaps measuring 3–4 cm in length—this method would seem to be the best. Then too, as in this case, it is all that can be tried when an operation is refused. However, I feel that when there is no vagina, or only a dimple 1 cm in depth, few women would continue these treatments long enough to make the method succeed, and, therefore, in many instances, an operation is preferable.

The third patient was a generally well-developed woman, age 32 who had never menstruated. She did, however, give a history of recurring

attacks of discomfort in the lower abdomen. She thought that perhaps the attacks came at monthly intervals, but she was not certain of this. Later developments in the case indicated that the supposed monthly periodicity of these attacks was probably due to suggestions on the part of the doctors who had examined her. On examination, the breasts were found to be normal. The clitoris and labia majora and labia minora were present and moderately well developed. There was an opening in the perineum just below the external urethra. It was about 1 cm in depth. Rectal examination showed a large mass of tissue in the pelvis which was fully the size of a normal uterus.

After examining the patient, I suspected that I was dealing with an entirely different condition than existed in the first two women. It seemed probable that this woman had a normally developed uterus which, as suggested by the monthly attacks of pain, menstruated and that the blood could not be discharged because of the absence of a vagina. The patient was told that there was a possibility that a vagina could be made and connected with her uterus so that she not only might have sexual relations, but might possibly menstruate and even conceive. This patient had been examined by several doctors before I saw her, and the consensus of opinion was that the mass palpated through the rectum was an enlarged uterus. However, permission was obtained to perform a celiotomy if indicated—which should always be done when one operates upon a patient with this condition.

I decided to follow the technic recommended by Wharton, in which an incision is made in the perineum, the tissues dissected by blunt dissection until a tunnel is produced, after which a vaginal form is introduced into this cavity. No attempt is made by plastic surgery to cover the newly formed cavity with epithelium as was done in my first case. In carrying out the Wharton operation on this patient, I made my dissection upward slowly until only about 1 cm separated the top of the newly made vagina from the large mass which I had felt on rectal examination, and which up to that time I had thought to be the uterus. This dissection upward was carried out until a vagina 7 cm in length had been made. At this point, I thought it wiser to make a lower abdominal incision and actually see the condition in the pelvis before burrowing further upward from below.

After making this incision, I was surprised to see that what I had thought was the uterus was the patient's only kidney. There was no renal tissue in either renal fossa. The pelvic kidney was one-half again the size of a normal kidney. One ureter could be felt extending downward on the left side towards the bladder, although the kidney itself was situated just about in the midline over the promontory of the sacrum. No right ureter was seen or palpated. The left ureter and ovary were normal. No right tube or ovary was seen. The uterus measured only 2 cm in length. There was no Meckel's diverticulum. The appendix was removed and the abdominal incision closed. The patient was again placed in the perineal position and a Wharton-form made of balsa wood was introduced into the newly formed vagina. The

patient remained in the hospital for about two weeks with the form held in place. After leaving the hospital, she continued to wear it for two weeks, and after that, wore it part of the time for three months. When the patient was operated upon, she thought she would marry in the next few months, but later decided to postpone the marriage because of the war. She stopped using the dilator against my advice. Two years later I saw this patient. The vagina was still 7 cm. in length, but the orifice had contracted down so that it would admit only one finger. It was, however, very easy to dilate the orifice under sodium pentothal, so that two fingers could be easily introduced. The patient is now using a vaginal dilator which she can introduce the full length without causing any discomfort. It measures 9 cm. in length, and has a circumference of 11.5 cm. When she marries she will have no dyspareunia.

In this case, there were embryologic defects in both the generative and urologic systems. It has been pointed out by several writers that when there is a defect in one of these two systems, one should be on guard for abnormalities in the other. In spite of this, I mistook, at least temporarily, the patient's only kidney for an enlarged uterus. If I had not recognized while operating, that I was dealing with something very unusual and had continued my dissection upward from the vagina, there is considerable likelihood that one of the large renal vessels might have been torn, with very serious consequences. In the future, in every case of absence of the vagina, I shall take a routine intravenous pyelogram before operating. In this instance, an intravenous pyelogram was not taken until after the operation. It showed that there were no kidneys in the renal fossae. The patient's only kidney could be seen situated down in the pelvis. It was poorly visualized because the dye drained so rapidly from the kidney into the bladder. One could, however, see quite plainly the left ureter which was not dilated. The patient's urine was negative on examination, and her renal function normal.

The fourth, and most recent, case was that of a 20-year-old girl, referred to me by Dr. Hugh Young. She had never menstruated. Her breasts were normally developed. The distribution of pubic hair was of the masculine type. The clitoris, labia majora and labia minora were normal. There was no sign of hermaphroditism. Just below the urethra there was a small depression 1 cm. in depth.

At an abdominal operation performed by Doctor Young, her uterus was found to be 2.5 cm. in length. The fallopian tubes were small and poorly developed. The ovaries were normal, and one ovary showed a graafian follicle. On palpation through the lower midline incision, Doctor Young found that the left adrenal gland was somewhat larger than normal. Whether this finding has any bearing on the congenital absence of the vagina is, of course, problematic, but it was an interesting finding and suggestive. The appendix was removed, and one week later I performed the following operation.

Operation—Johns Hopkins Hospital—December 13, 1943. An inverted U-shaped incision was made through the skin, beginning just below the

urethra and extending backward, and slightly laterally, until the dorsal ends of the incision terminated 2 cm ventrally and laterally to the anus (Fig 1) This incision was then continued through the subcutaneous fat for about one cm Then, beginning at the ventral border, the tissue was undercut from above downward forming a flap whose pedicle was the tissue in front, and just lateral to the anus (Fig 2)

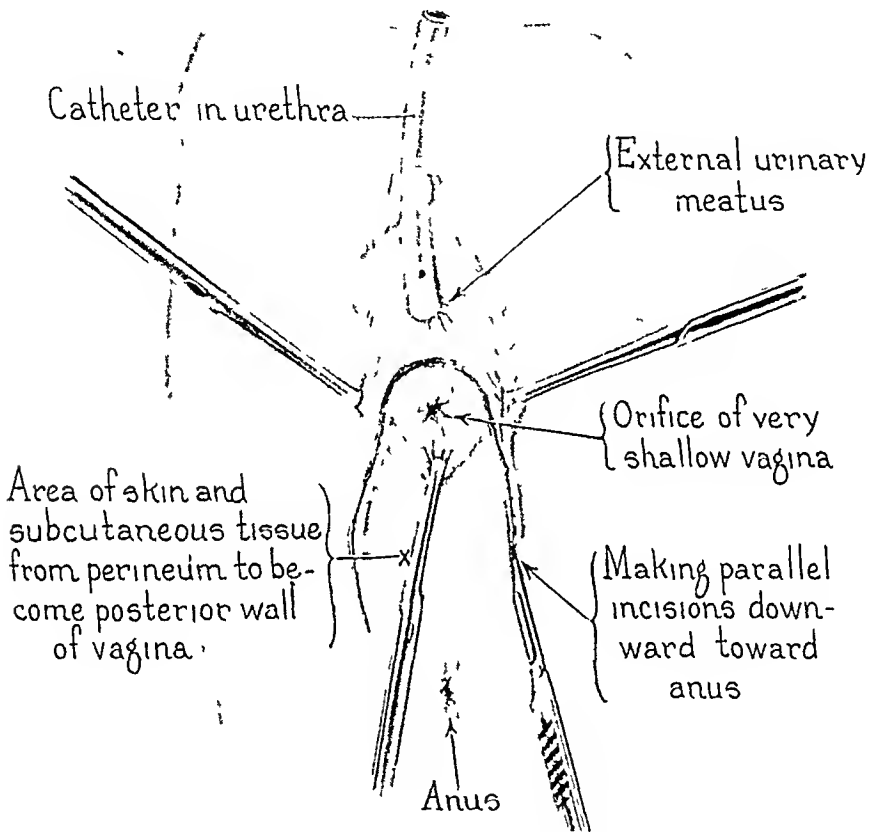


FIG 1.—An inverted U shaped incision has been made through the skin beginning, just below the urethra and extending backward and slightly laterally until the dorsal ends of the incision terminated 2 cm ventrally and laterally to the anus

After turning this flap backward, the fat and subcutaneous tissue under it were carefully separated and stretched by blunt dissection until there was a cavity into which two fingers could be introduced for a distance of 8 cm In carrying out this dissection, the operator took special care not to come too close to the urethra, bladder or rectum A retention catheter had been introduced into the bladder, and a rectal tube into the anus before the operation was started and, by means of these, it was possible to tell just how closely the dissection approached the urinary and intestinal tracts In this case, there was never any danger of the urethra or bladder being injured However, as the dissection was carried upward, the rectum seemed to be getting nearer and nearer until only a small amount of tissue separated it from the cavity

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that was being formed. Because of this, the dissection upward was stopped when the cavity measured 8 cm. There probably is in different cases considerable variation in the extent that the rectum bulges anteriorly toward the space that ordinarily would be occupied by the vagina. In the other women for whom the operator has made vaginas, there was not the danger of injuring the rectum that there was in this case. Now that a cavity 8 cm in depth, and of sufficient diameter to admit two fingers, had been dissected out the steps remaining in the operation were

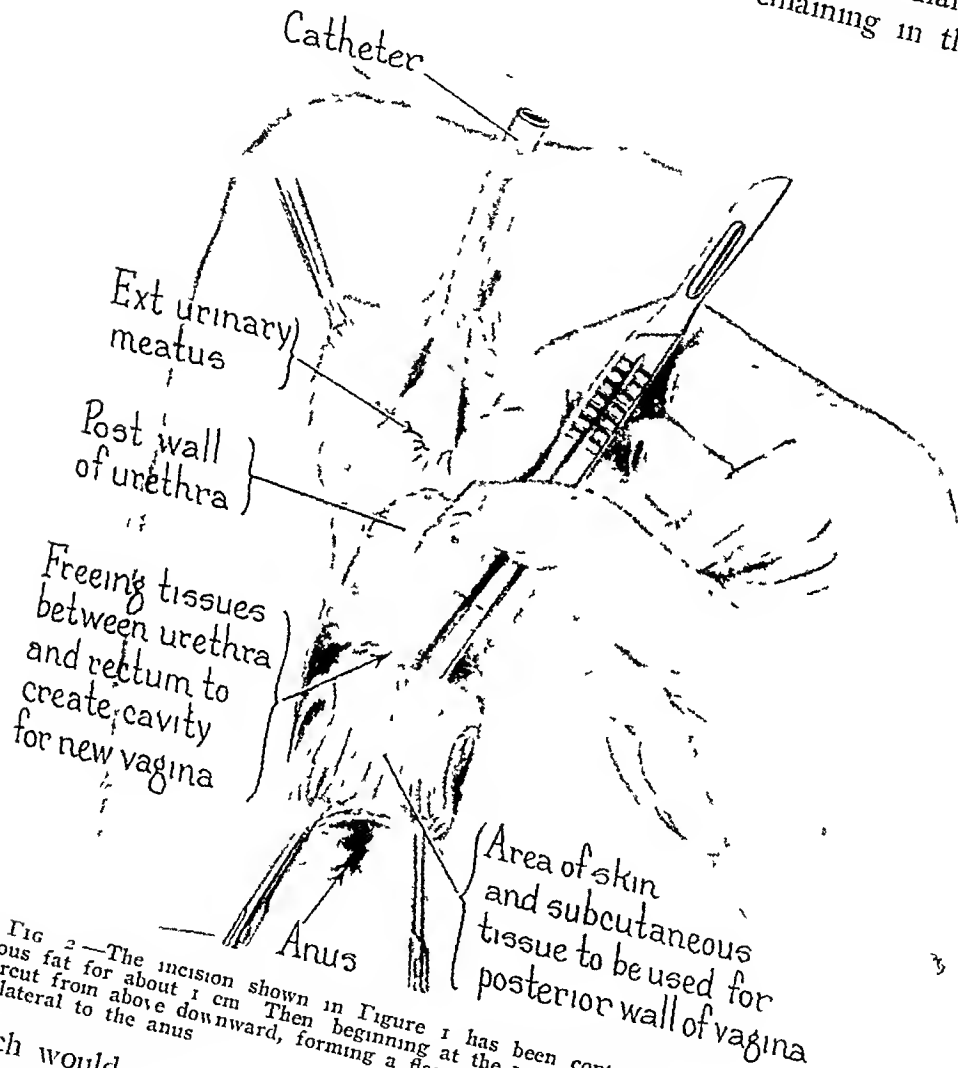


FIG. 2.—The incision shown in Figure 1 has been continued through the subcutaneous fat for about 1 cm. Then beginning at the ventral border, the tissue has been undercut from above downward, forming a flap whose pedicle is the tissue in front and just lateral to the anus.

those which would cover as far as possible, this cavity with epithelium and which would prevent its postoperative obliteration through contraction. The first step in accomplishing this was to carry the U-shaped flap of skin and subcutaneous fat which had been made by the original incision deep down into the cavity and sew it to the underlying tissue. No chromic catgut sutures were used for this fixation (Fig. 3). The operator had never before made a flap to cover the posterior wall of a newly made vagina in just the way done in this case, nor had he read of this procedure in the literature. The

flap measured about 6 cm in length. By extending the ends of the original incision practically to the anal margin, this flap might have been made 1 or 2 cm longer.

To cover the anterior and lateral walls of the vagina, the labia minora were dissected off from above downward in such a way as to leave pedicles sufficiently large to furnish good circulation. The available mucous membrane in each flap was increased by splitting apart from below the surfaces

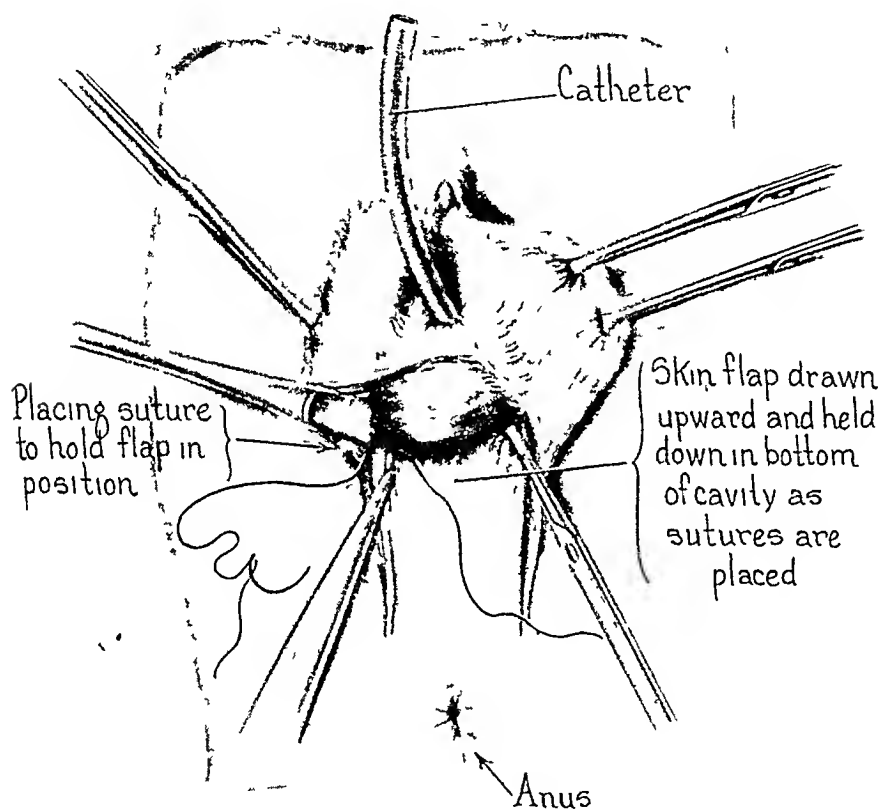


FIG 3—The U shaped flap of the skin and subcutaneous tissue shown in Figure 2 has been carried deep down into the cavity and is being sewed to the underlying tissue.

of each labium minus, thus, converting the large folds into flat surfaces (Fig 4). These flaps were then sewed deep down into the vagina with zero chromic catgut. The raw areas left by dissecting away the labia minora were then covered by sewing together the adjacent skin surfaces with interrupted sutures of chromic catgut. Care was taken, both in making these flaps and later in covering all the raw areas, not to injure in any way, or encroach too closely on the clitoris.

It was then evident that a vagina, 8 cm in depth, had been made whose anterior and lateral walls were well covered with epithelium, except for a very narrow area in the anterior midline. The lower two-thirds of the posterior

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wall were also covered by an epithelial flap (Fig 5) The only raw area that remained was in the uppermost part of the posterior wall To cover this with epithelium, Dr Edward Hanrahan then cut a midthickness split-graft, measuring 11 x 5 cm, from the right thigh This graft was sewed over a Wharton "vaginaform" made of balsa wood, then introduced into the vagina in such a way that it was in close contact with the remaining uncovered

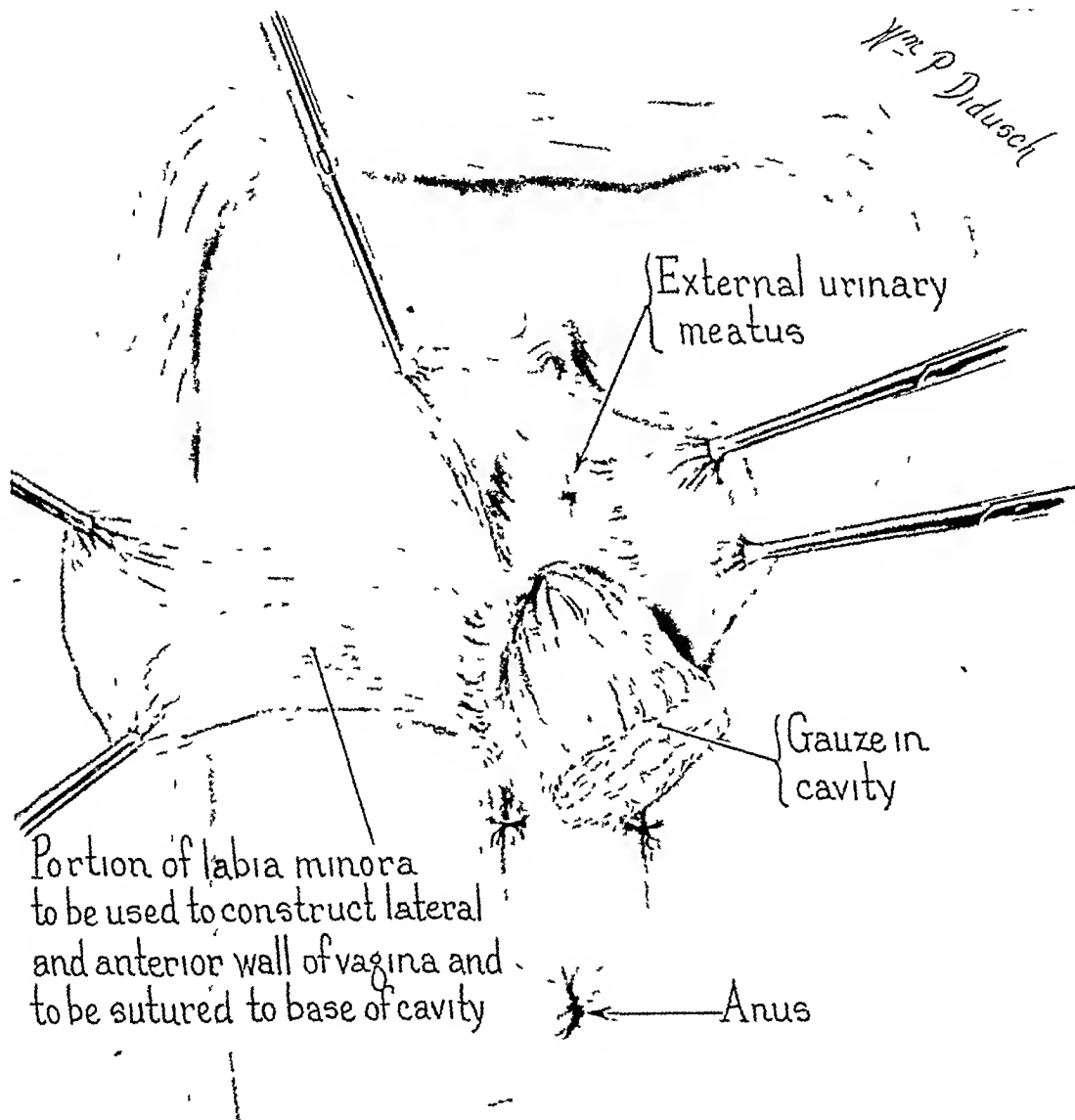


FIG 4—The labia minora are dissected off from above downward in such a way as to leave pedicles sufficiently large to furnish good circulation The available mucous membrane in each flap is increased by splitting apart from below the surfaces from each labium minus, thus, converting the large folds into flat surfaces On the right is shown the large flap that can be made in this way

area A retention catheter was left in the bladder The patient left the operating room in good condition There had been very little loss of blood

The patient's convalescence was satisfactory, although she did complain of the discomfort caused by wearing the "vaginaform," which was removed on the tenth day It was then evident that the flap made from the skin of the perineum by the converted U-shaped incision had lived, and that it now

covered the lower two-thirds of the newly made vagina. The flaps formed from the labia minora were also living completely covering the lateral vaginal walls. It was difficult to be certain how much of the graft cut from the right thigh survived, but certainly some of it did. The patient left the hospital on her 12th postoperative day, but remained in the city for a month longer, coming to my office three times a week. On her last visit, the vagina

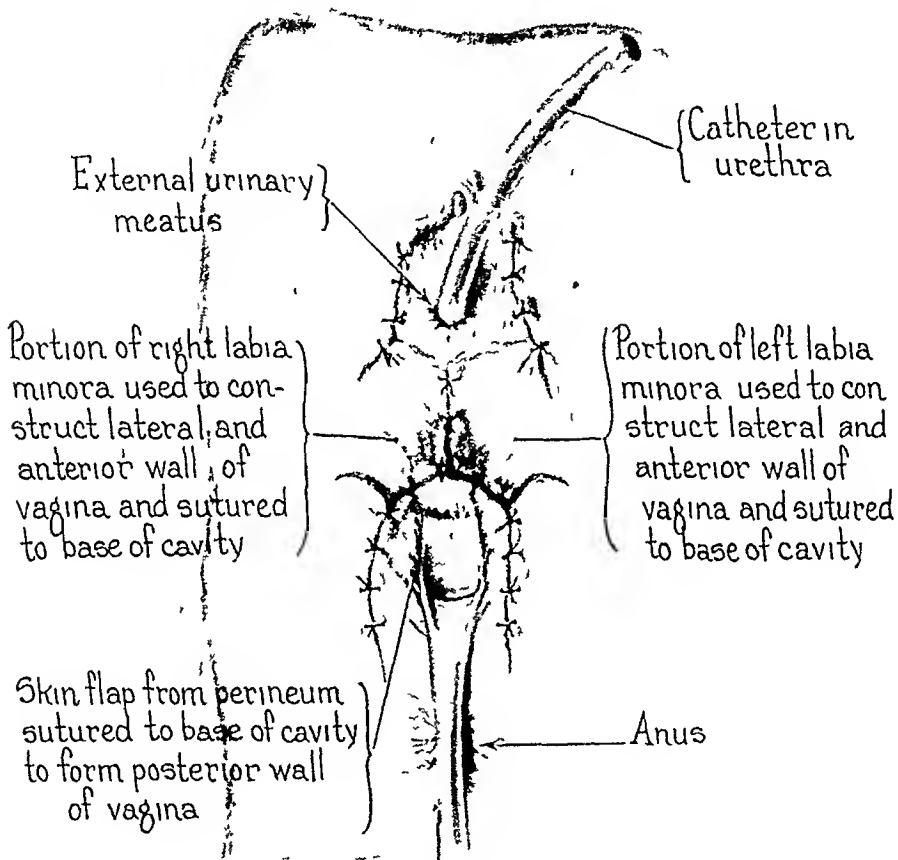


FIG. 5.—A vagina 8 cm. in depth has been made. By using a flap of skin and subcutaneous tissue, practically all of it has been covered with epithelium.

easily admitted two fingers. She is now using a vaginal dilator which she can introduce the full length without causing any discomfort. It measures 9 cm. in length and has a circumference of 11.5 cm. When she marries she will have no dyspareunia.

SUMMARY

Vaginas were made for four women. The method used in each case was different. In the first, the labia minora were unusually long, and by utilizing them, it was possible to cover over most of the newly made vagina with epithelium. In the second case, a vagina which has proven satisfactory for several years was made without any operation. The intelligence and cooperation of this patient played a large part in making this procedure successful. In the third case, the Wharton technic was followed. This

consisted in making an elongated canal in the perineum and keeping that tube open by means of a vaginal form of balsa wood. Following the technic Wharton first recommended, no effort was made to cover the newly made vagina with epithelium. In the fourth case, an extensive plastic operation was performed in which the labia minora were again used to cover over raw areas, but as they were not long, this step was supplemented by using the skin of the perineum between the urethra and anus. This was accomplished by making an inverted U-shaped incision, dissecting out a flap between the urethra and the anus, and sewing this flap deeply into the newly made vagina.

The third case in this series was particularly interesting, as in addition to the embryologic abnormalities of the generative tract, there was also an abnormality of the urologic system. The patient's only kidney was low in the pelvis and was mistaken by several examiners for the uterus. There probably is no one best method of making a vagina. In the writer's opinion, one should take into consideration the anatomic findings, the temperament, intelligence and marital status of a patient.

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SPONTANEOUS PERFORATION OF THE RECTOVAGINAL SEPTUM, FIVE WEEKS AFTER CONSTRUCTION OF THE VAGINA*

CASE REPORTS

LAWRENCE R. WHARTON, M D

BALTIMORE, MD

CONSTRUCTION OF THE VAGINA involves the dissection of a large space between the rectum and bladder. This dissection is usually easy, unless operations have been performed in this region before. If there have been former unsuccessful attempts to construct the vagina, the normal plane of cleavage is replaced by dense scar tissue. This makes the dissection extremely difficult and, under these circumstances, injuries of the rectum or bladder have been common and unavoidable. These accidents have occurred during the course of the dissection, in the operating room. In the case herewith reported, however, the perforation occurred 5 5 weeks after a successful operation and convalescence, and was due to the pressure of the strong perineal muscles on the vaginal form which pushed the vaginal form through the vaginal wall into the rectum. This is the first complication of this sort that I have encountered. It is my purpose to analyse the factors that caused this disastrous accident, in the hope that we may, in the future, prevent them.

Case Report—The patient, age 24, had undergone the vicissitudes that are so often experienced by women who have no vagina or uterus. At the age of 15, because of her failure to menstruate, she had a gynecologic examination. At that time, she was called normal, the amenorrhea was deemed functional, and attributed to the high altitude of Colorado Springs. A shift to low altitude did no good, although the young girl continued to develop normally in every other way. For three years, from the age of 17 to 20, she received hormone injections. When she wanted to get married, at the age of 24, she did not have a premarital examination, she assumed that her menstrual periods would appear after marriage. After her marriage, however, she made the further unfortunate discovery that she could not have coitus. It was not until this time that a careful gynecologic examination was made, which revealed the true state—complete absence of the vagina and uterus.

A few months later, in November, 1943, she came to Baltimore. She was a perfectly normal and healthy young woman whose sole defect lay in the complete nonunion and developmental inhibition of the müllerian ducts, resulting in complete absence of the vagina and uterus. The ovaries and secondary sex characteristics were normal. Since the indication seemed clear, a vagina was constructed using the basic technic I described in 1938. I lined the vaginal space with skin, using a Thiersch graft cut from the thigh. The skin graft was cut by Dr. E. M. Hanrahan. The graft was sewed over the vaginal form. The operation was performed November 11, 1943, at the Johns Hopkins Hospital.

Five and one-half weeks later, after the patient had been out of the hospital for two weeks, she returned for an examination. She was still wearing a vaginal form. The vaginal cavity was 11 cm deep, large, and completely lined by epithelium except in the vertex. We thought we had accomplished an almost perfect result. At this follow-up examination, I removed the form easily, replacing it by a smaller vaginal form which the patient had worn before with perfect comfort. I was so pleased with the result that I arranged for her to return to the hospital the following morning, when I could demonstrate the result to one of my associates.

* Read before the Fifty-sixth Annual Session of the Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

VAGINAL CONSTRUCTION

Twelve hours later, during the night, the patient felt a desire to defecate, and in spite of using great pelvic pressure, was unable to do so. She noted the passage of a certain amount of bloody discharge from the vagina, although there was no pain. From her hotel, she called the resident gynecologist who asked her to call me the following morning.

When I examined her the following morning, the form was so high in the vagina that I could just touch it with the index finger. Also, the perineal muscles and vaginal orifice were so strongly contracted that it was impossible to remove the form without an anesthetic. A small amount of sodium pentothal was therefore given, the constrictor

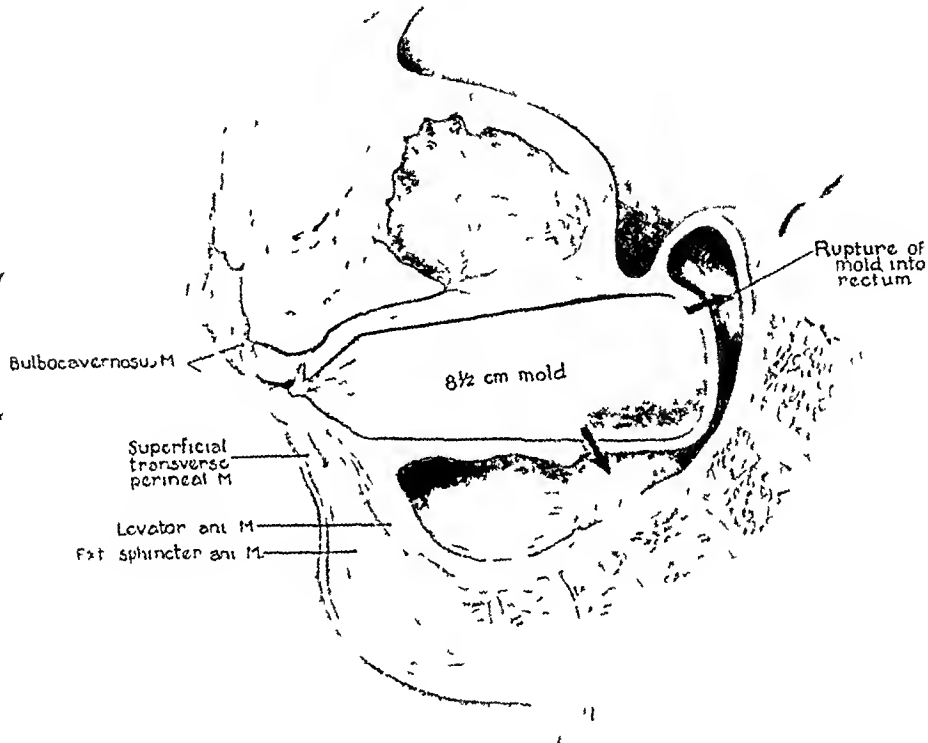


FIG 1—The figure shows the position of the form in the constructed vagina. It is not visible from the vaginal orifice. Pressure of the perineal muscles and the pelvic diaphragm is exerted on the end of the form and this may force the form into the rectum or the peritoneal cavity. This illustrates the reason for using a form that is either much shorter than the above or definitely longer.

muscles of the vagina and the proximal fibers of the perineal fascia were cut, and the form removed from the vagina. The apex of the form was seen to be covered with fecal material, it was, therefore, evident that the end of the form had been forced through the rectovaginal septum into the rectum. The opening into the rectum admitted two fingers, and was in the apex of the newly constructed vagina.

The repair of the large rectovaginal fistula immediately became the chief problem, and to cure it, we had to sacrifice part of the vagina which we had so carefully constructed. I inserted a large tube into the rectum, through the anus, and closed the rectovaginal opening over this tube. The fistula was closed very loosely, using only three interrupted sutures of No 0 chromic catgut. This merely brought the torn edges of the rectovaginal septum into contact with each other, so that they could heal. The vaginal cavity was then irrigated and packed with xeroform gauze.

The subsequent care consisted only of keeping the rectal tube in place for about two weeks, and keeping the vaginal space as clean and open as we could. We allowed the walls of the apex of the vagina to adhere to each other, to close the rectovaginal

fistula Within six weeks the fistula was closed completely After this, the vagina was examined every week by me, and dilated every night by the patient, using a form which we gave her Nine months after the accident, the vagina was seven centimeters deep, admitted three fingers easily, and was everywhere lined by normal epithelium This provided a vagina about two-thirds as deep as it had been before the accident occurred But it was a deeper and more commodious vagina than had usually resulted following the employment of other, more complicated operative techniques

COMMENT —From the above experience, I would draw the following conclusions

1 The vaginal form should never be so short that it lies completely above the muscular plane of the pelvic diaphragm In this case, I noted that the vaginal form was so short that it disappeared completely in the large vagina Hence, any pressure exerted by the pelvic floor was directed against the end of the form and pushed the form higher against the rectum or cul-de-sac of Douglas One safeguard against this accident would be to have the form long enough to protrude slightly from the vaginal orifice A form of such length could not be pushed upward by perineal pressure

2 A second safeguard against this accident would be to make the vaginal orifice so large that it could not close or contract over the end of the form It should be large enough to allow the form to escape if the intra-pelvic pressure is increased It should always be easy to reach and remove the vaginal form The vaginal orifice can be enlarged easily by cutting the constrictor vaginae muscle and the proximal fibers of the perineal fascia This also prevents dyspareunia later

3 Constipation is to be avoided The patient in this report had been constipated If constipation should develop the patient should avoid pressure to produce defecation

4 The method of closure of the fistula was simple We made no attempt to dissect out the layers of the rectovaginal septum, we only provided a loose approximation of the torn edges, and put the whole region at rest by a large rectal tube In spite of the unfortunate accident, the ultimate result was not entirely unsuccessful

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DISCUSSION —DR HOWARD MAHORNFR, New Orleans, La I am interested in these papers because I have had an opportunity to construct artificial vaginas in two women Doctor Wharton deserves credit for calling attention to the fact that it is possible to construct a vagina by a procedure relatively simple compared to the older methods of intestine transplant Since I heard his presentation and the description of his method before this Association, I have operated upon two cases My idea, also, in this discussion is to present a stent which was used on my patients

In devising the stent two ideas seemed important, one, to obtain a satisfactorily large vagina so that if there was any contraction there would still be ample space, and two, to protect the urethra, which would be endangered by pressure if the stent used was large I had a machinist construct this stent, which is shaped like a radio tube In the front of it is a large groove which permits the use of an indwelling catheter in the urethra to remain without fear of pressure necrosis The stent is six inches long and two

VAGINAL CONSTRUCTION

and one-quarter inches in diameter. In preparing the space at operation I have found the dissection between the rectum and bladder very much like that required in this region for abdomino-perineal resection. One need not be afraid of dissecting very high and of making a huge space. The stent can be worn for a long period of time if necessary.

A split-skin graft was placed on the stent. The take was remarkable (Fig 1). This is the largest size speculum which after healing is admitted easily, and one could put the fingers into the vagina and by bimanual examination feel them easily just under the abdominal wall. The lower part of the vagina did not heal promptly. Because of this it was necessary for her to wear the stent for months. The lower area was regrafted and shortly after that she was married and found the stent was no longer necessary. She assured me her marital relations were happy in every respect.

Avoidance of scar tissue by early skin graft is important. In the second patient the stent was worn only a short time (three weeks). The stent is connected with rubber bands to an abdominal belt made of canvas.

I am glad to see Doctor Brady's procedure because I think the method may be helpful in preventing contractures at the vaginal outlet.

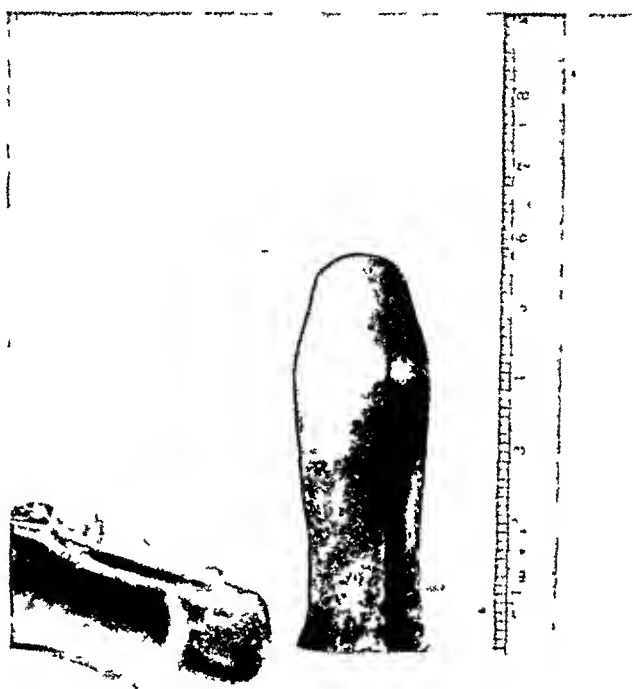


FIG 1.—Stent for use in constructing an artificial vagina. A groove cut anteriorly on the stent protects the urethra in which, in the initial postoperative period, is an indwelling catheter. Otherwise, there may be danger of pressure necrosis from so large a stent. Anteroposterior holes at the base of the stent permit rubber tubes to be passed through which are attached to an abdominal girdle. The stent is very large, approximately six inches in length and two and one-quarter inches in diameter. It is shaped like a radio tube. The large size is to insure against contraction. It is covered with a split thickness graft and inserted into the new space.

DR. LEO BRADY, Baltimore, Md (closing) I agree that it is usually easy to make as long a vagina as you desire. However, in an occasional case there is danger of getting into trouble. In one of my patients there was no difficulty in keeping away from the bladder and the urethra, but as the dissection was extended upward, the rectum came closer and closer to the operative field. Apparently in different patients, the extent to which the rectum bulges forward into the area normally occupied by the vagina varies considerably.

DR. LAWRENCE R. WHARTON, Baltimore, Md (closing) I agree with Doctor Mahorner about the grafts. We have used Thiersch grafts in these cases, there is much more rapid healing and scar tissue is abolished. The large outlet I think is important. The operation is useless if the vaginal opening is not satisfactory and ample.

INTERVERTEBRAL DISK LESIONS ARE THE MOST COMMON CAUSE OF LOW BACK PAIN WITH OR WITHOUT SCIATICA*

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SO-CALLED IDIOPATHIC low back pain with or without sciatic radiation is the most frequent condition seen in the adult orthopedic clinic. In spite of the fact that orthopedic surgeons have devoted much time and thought to this condition, the pathologic changes which are responsible for the symptoms are, for the most part, unknown. Consequently, the diagnosis of low back conditions is largely a matter of speculation. Hundreds of articles have been written on the subject and many classifications of low back pain have been offered. Over 20 years ago a diagnostic study of a series of 300 patients whose principal complaint was low back pain or sciatica led me to conclude that the great majority of these patients were suffering from strains of the lumbosacral or sacroiliac joints (Key¹). In spite of the fact that half of these patients were studied in Boston, where the sacro-iliac joint was then at its zenith as a cause of low back pain, the lumbosacral strains were found to outnumber the sacro-iliac strains by over four to one. It was further stated that while about one-third of the patients presented evidence of hypertrophic arthritis in the roentgenogram, the pain was not due to the arthritis *per se*, but was caused by strain.

The patients were classified as follows:

- 1 Lumbosacral strain of sudden onset (pain predominantly unilateral in the low back and often referred to the superior gluteal and sciatic nerves), 35 to 40 per cent
- 2 Lumbosacral strain of gradual onset (pain as in 1), 20 to 25 per cent
- 3 Postural type of lumbosacral strain (pain midline and bilateral in the low back and not referred), 20 to 25 per cent
- 4 Sacro-iliac strains, 15 to 20 per cent

It was stated that the pathology of the above conditions was not known, but it was suspected that the lesions of traumatic and gradual lumbosacral strains were true sprains with tearing or stretching of the ligaments or joint capsules and that the referred pains were due to irritation of the nerve roots by synovitis or exudate in the adjacent joints. It was further stated that the prognosis in all of these low back strains was, as a rule, good, but that chronic and recurring cases usually require a longer time for cure.

In the intervening 20 years I have read a considerable part of the voluminous literature on low back pain and sciatica, but until recently I have not been sufficiently impressed to adopt any important changes, either in the classification or methods of treatment outlined in that paper, except that I have grad-

* Read before the Fifty-sixth Annual Session of the Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

ually eliminated the sacro-iliac strains. At no time have I accepted the various current explanations of low back pain, such as fascitis, insufficiency of the vertebrae, facet syndromes, instability of the lumbosacral spine, tight fascia lata, fibrositis, sacralized transverse processes and other congenital anomalies in this region, spondylitis, sacro-iliac subluxations, apophyseal subluxations, apophyseal arthritis, ligamentous strains in this area, focal infections, *etc*

When Barr and Mixter² reported their work on protrusion of the nucleus pulposus, I, like most orthopedic surgeons, agreed that they had discovered the cause of the pain in a small percentage of the patients with low back pain and sciatica, but I was not at all interested in turning my patients over to a neurologic surgeon in order that he might inject lipiodol and search for a filling defect in their spinal canals. What happened to those patients in whom no filling defect was found? In what percentage of the spinograms were the examinations negative? Did these patients develop symptoms caused by the lipiodol? Did patients with protruding disks get well without operation? In vain I watched the literature for answers to these questions and also for convincing reports on the end-results of disk operations.

Our patients with low back pain had been getting along pretty well and the first duty of the physician is to do no harm. Experience had shown us that the great majority of our patients with low back pain, with or without sciatica, either continued their normal activities during the period of pain or were able to resume them after a variable period of conservative treatment at home and the more resistant cases were hospitalized and a very few of these were operated upon as a last resort. But conservative treatment and time were given a chance to effect a cure before surgery was even contemplated. The lipiodol injection and spinogram seemed to me to be a rather formidable procedure and I wanted none of it in my practice.

When Spurling, Dandy, Semmes, Love and other neurologic surgeons began operating upon these patients on the basis of the history and physical examination, I became seriously interested in the subject and learned to perform the operation. As practically all of my disk operations are done under local anesthesia, I soon discovered why orthopedic surgeons had not discovered disk protrusions long ago. It is because they had done little or no work in the spinal canal and did not know or appreciate the significance of the fact that the nerve roots within the canal are exquisitely sensitive as compared with the peripheral nerves. Realization of this fact immediately focuses one's attention on an intraspinal cause when dealing with referred pain and it is found that a relatively slight lesion within the canal can cause severe symptoms.

It soon became evident that the protrusion of the disk was a satisfactory explanation of the symptoms in patients with the typical disk syndrome, but what of all of the other patients with low back pain of varying degree and in whom the pain may be localized in the low back or at times be felt in the buttocks, thigh, leg or foot? If these are not disk lesions, what are they?

Even before I accepted a lesion of an intervertebral disk as a frequent

cause of this condition, I had gradually eliminated sacro-iliac strains as a cause of low back pain and sciatica. This left the traumatic and the postural type of low back pain. Both originate in the lumbosacral area (fourth and fifth lumbar and first sacral vertebra) and may be of sudden or gradual onset and begin with or without known cause. In the traumatic type the pain is predominantly unilateral and also tends to be referred to the buttocks, posterior thigh, calf and even to the toes. In the postural type the pain is in the midline and bilateral in the lumbosacral region and tends not to be referred.

The physical findings in these patients vary directly with the severity of the symptoms present at the time of the examination and all transitions exist between the patient with a complaint of mild unilateral low back pain who is completely negative on physical examination and one with a typical disk syndrome with severe back and sciatic pain, marked muscle spasm and pain on movement, limitation of movement of the back and lower extremities and sensory and reflex changes in the involved lower extremity.

It is further to be noted that the symptoms may vary greatly from time to time and even from day to day and while in some patients the symptoms and signs may persist for weeks or months, in others even 24 hours' rest in bed may produce a marked change in the clinical picture. It, thus, may be possible to trace the various transition stages between the mild unilateral low back pain and the typical disk syndrome in a single patient if he is studied over a period of time and his symptoms become aggravated or subside during the period of observation. Since the above is true, why are not all of these traumatic type of lumbosacral strains due to lesions of an intervertebral disk? No other cause has ever been demonstrated. As is stated above, it is pure speculation to attribute the symptoms to any of the various diagnoses under which these conditions have been treated in the past. A disk lesion is the most logical explanation of the dramatic relief which is sometimes obtained by manipulation of the low back.

The postural type of lumbosacral strain is characterized by a history of pain in the midline and across the low back and this pain is not referred to the lower extremities. On physical examination these patients exhibit tenderness on pressure in the lumbosacral region and the pain is aggravated by hyperextension of the low back. In most instances the symptoms are not very severe and the patients do very well under conservative treatment. However, in an occasional patient with a lumbosacral strain of the postural type operative treatment is advisable and in about 25 such instances I have explored the spinal canal in the lumbosacral region and have found and removed disks which protruded in the midline and in most, if not all, of these the operation was followed by relief of the pain. These cases are similar to those reported by Dandy.³

In the postural type lumbosacral strains also there are all transitions between the mild and the severe cases and it may be possible to follow the changes in a single patient if he is examined at intervals while his symptoms

are becoming quiescent or aggravated. If this is true, why are not all of these postural types of lumbosacral strains caused by lesions of an intervertebral disk? Certainly no other cause has been demonstrated. Twenty years ago I wrote vaguely of "irritation of the posterior sacrum caused by pressure of the articular processes of the last lumbar vertebra which in hyperextension glide down over their facets to impinge on the sacrum" (Key¹). This was unsatisfactory then, but nothing better has been offered until we have realized the frequency and significance of lesions of the intervertebral disks. There is no question but that the intervertebral disk is not only subject to degenerative changes, but it is the most vulnerable structure to injury in the low back.

It is, thus, evident that I now believe that in practically all patients with idiopathic low back pain the cause of the pain is within the spinal canal and that in over 90 per cent of the cases this is a lesion of the intervertebral disk. It is probable that in many of the mild cases the back pain originates in the disk itself, because frequently at operation under local anesthesia pain has been produced by pressure on the disk or on the adjacent periosteum or ligament or by manipulating an instrument within the disk and thus moving the adjacent vertebrae. Also, it is significant that in most instances the back pain appears first and the gluteal or sciatic pain begins some days or weeks later or may not appear until after one or more episodes of back pain. It is possible that some of the back pain is due to irritation of the nerve roots and is referred along the posterior primary division of the involved spinal nerve.

The problem of diagnosis, then, is first to determine whether or not the patient's pain originates in the low back. This can be done by the history and physical examination. In my experience if pain in the low back is the dominant symptom the pain is rarely caused by genito-urinary or pelvic disease. Many gynecologists and urologists have spoken and written freely on gynecologic and kidney or prostatic low back pain, but I practically never see these patients. If the pain is in the lumbosacral region and this area is tender on deep pressure and if the pain is aggravated by certain movements of the low back or lower extremities, then it originates in the low back. The exceptions are so rare as to be negligible for all practical purposes. Malingering and psychoneurotic backache must be ruled out, but these are not considered as a part of idiopathic low back pain.

If the pain originates in the low back it may be due to a destructive disease of the bone, such as a neoplasm or tuberculosis, to an ankylosing arthritis or to a caudal tumor, to a fracture, or to a spondylolisthesis, and I suspect that in spondylolisthesis the pain is due to the lesion in the disk. All of these conditions, except caudal tumors, can be diagnosed roentgenologically, unless they are examined very early in the disease. As a group, they comprise less than 10 per cent of the cases of low back pain and over half of these are spondylolisthesis and less than a tenth of them are caudal tumors. c

This leaves over 90 per cent of the patients with low back pain and over 98 per cent of those with so-called negative roentgenograms in the idiopathic group. It is my opinion that in all of these the lesion is intraspinal in origin.

and is due to a lesion of the intervertebral disk. No other pathology has ever been demonstrated as the cause of the pain. It is understood that hypertrophic arthritis, a thickened ligamentum flavum, congenital anomalies of the spine and so-called unstable lumbosacral joints and the other conditions mentioned above are rejected as causes of low back pain. The diagnosis is made from the history and physical examination and no lumbar puncture or spinogram is necessary or even advisable. Roentgenograms may offer confirmatory evidence in that if the lesion is chronic or recurrent the involved disk may be narrowed and the adjacent bone may be eburnated and its margins may be hypertrophied. This ridging of the posterior margin of the vertebral body is considered a part of the disk lesion.

This does not mean that all of these patients should be operated upon and the offending disk or disks removed. As a matter of fact, in only about 10 per cent of these patients is an operation the treatment of choice. In the great majority of them the symptoms either subside spontaneously or yield to conservative treatment and in the remainder the pain and disability are not sufficient to warrant the operation.

It may be argued that in many of these patients no rupture or obvious protrusion of the disk is found at the operation. This does not prove that the disks were normal and Dandy's⁴ concealed disk is a very real and important contribution to this phase of the problem. I, with many others, have been too slow in accepting it. Its recognition permits the surgeon to operate with more assurance that the cause of the patient's pain will be found and relieved.

It is also argued that some patients continue to have pain after the operation. This, too, is true and can be explained by (1) incomplete removal of the offending disk, (2) removal of the wrong disk or of only one disk when two or more are causing symptoms, (3) recurrence or protrusion of more disk material from the operated disk, (4) later protrusion of a neighboring disk, (5) the presence of a ridge of bone at the margin of the offending disk, (6) adhesions following the operation, (7) arachnoiditis or nerve damage from pressure by the disk, and (8) a tumor may have been missed. Many of these unrelieved cases should be operated upon a second time and at this operation a hemilaminectomy should be performed if necessary, and the lower lumbar canal explored thoroughly in an effort to find and remove the cause of the pain. In my experience a spinal fusion has not relieved the pain in patients who have persistent pain and disability after an unsuccessful disk operation and I have now abandoned this procedure as a cure for idiopathic low back pain.

The spinal nerve roots lie close to the anterior wall of the canal and are not subject to pressure by a thickened ligamentum flavum or the lamina. It is thus difficult to explain the relief sometimes obtained by the so-called decompression operations. The relief may be due to the careful freeing up of the nerve roots rather than to the decompression.

The diagnosis of idiopathic low back pain is no longer a problem, because

the term is synonymous with a lesion of an intervertebral disk in the affected area. And the same is true of most of those vague unexplained pains in the cervical and dorsal regions in which no pathology or only hypertrophic changes in the vertebrae can be demonstrated. As stated above, hypertrophic changes in the vertebrae are not the cause of pain unless we include the ridging of the vertebral margins beneath the nerve roots which sometimes occurs in old chronic disk lesions, and I consider this part of the disk lesion. It is not the same as the marginal lipping which is so commonly seen in the roentgenogram and does not occur unless the disk is damaged. There will, of course, be an occasional rare exception to this rule.

It is, thus, immediately recognized that the patient with idiopathic low back pain with or without sciatica has a lesion of an intervertebral disk and the problem is to relieve his symptoms in the simplest and safest manner. If our conservative measures fail we can then resort to surgical removal of the cause of the pain and offer him a reasonable chance of a cure. This point of view must be accompanied by the knowledge that in many of these patients the symptoms subside spontaneously, and the firm conviction that in most of the others they can be relieved by conservative treatment. The fact that they may recur is not an adequate reason for operation unless the recurrences have been so frequent and severe that the patient's comfort and welfare are seriously affected by the condition. The operation is an elective major surgical procedure and should not be undertaken lightly.

CONCLUSION

The conditions which we have called low back strains and classified as idiopathic low back pain are lesions of the intervertebral disks in this area.

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DISCUSSION—DR. GEORGE E. BENNETT, Baltimore, Md. You have just heard a keynote address on one of the planks of the platform of low back pain. It is very interesting that Doctor Key has keynoted on the same subject on different occasions. It is also interesting to have him summarize his statements with the fact that a large percentage of cases of low back pain are the result of disk lesions but that only ten per cent require operative interference. This statement we should weigh well. I should like to be here about 20 years from now, as I believe Doctor Key would retract some of the statements he made today, as he did some of the statements he made 20 years ago.

I do not wish to discuss the pros and cons of disk lesions. I have one of the cervical spine. I have had symptoms for 20 years and am still doing pretty well, and no neurosurgeon I know wishes to operate upon it. This is a broad subject and I believe orthopedic

surgeons, by and large, are very grateful for the monumental work done by neurosurgeons in helping us in a certain percentage of backaches which, to us, are headaches

DR PAUL B MAGNUSON, Chicago, Ill There are many things in medicine which we cannot explain definitely, nor can we always put our finger on the exact cause of symptoms However, it does seem that a careful analysis should be made of all possible causes of pain in any given location I have no doubt that Doctor Key believes what he says at this time, but I think, with Doctor Bennett, that we may hear him retract his statements, or very materially modify them, in a few years from now

It is surprising to me to hear a man of Doctor Key's knowledge and experience explain the common symptom of low back pain on the basis that it is usually due to rupture of an intervertebral disk Having known Doctor Key for a good many years, I am sure he knows the anatomy of the lower back, and also the pathology He is familiar with the tissues that make up the lower back, and the mechanical strains that are inflicted upon them, and he knows the conditions that cause pain in other joints of the body This being true, how he can glibly ignore the anatomic facts and calmly make the statement that the chief cause of low back pain is ruptured intervertebral disk, is more than I can understand

A study of the lower back would indicate that the tissues involved in its anatomy are the same as those in other joints, controlled by muscles and supported by ligaments the main difference being that these tissues are more closely in contact with peripheral nerves and their exits, and that the nerves lie in closer proximity to the supporting structures of the back than is the case in most other locations The ligaments here are more easily strained because of the tremendous leverage put upon them It occurs to me that we must use common sense, as well as analytic skill and patience, in making our examination, and consider the patient as a whole and not just a pain in the back

It would be very easy on a doctor's mentality if he could attribute all pain in the upper right quadrant to gallstones and send the patient to the operating room without further to-do In my opinion, there is just as much logic in sending a patient to the operating room with a diagnosis of ruptured intervertebral disk, because he has a pain in the low back accompanied by sciatica

The title of this paper is "Disk Lesions are the Chief Cause of Low Back Pain"—let's make a comparable statement "All kittens born in an oven are biscuits!"

DR GUY A CALDWELL, New Orleans, La Doctor Key has presented a highly speculative problem Apparently, his speculations were prompted by a discovery made while performing a laminectomy for removal of a ruptured intervertebral disk under local anesthesia, he noted that on poking an instrument into the disk and prying it against the ligaments he could produce low back pain similar to that of which the patient complained This finding, which has been previously commented upon by several neurosurgeons, together with the history that is often obtained in such cases, that intermittent periods of low back pain precede the onset of sciatic pain, constitutes the evidence favoring the hypothesis that ruptured intervertebral disks are the chief cause of back pain I admit that these facts strongly suggest that pressure of a protruding nodule of cartilage against the intervertebral ligaments is the probable cause of the low back pain which precedes the sciatic pain in proved cases of ruptured disk However, I cannot believe that *all* back pain is caused by degenerated disks trying to force their way through the intervertebral ligaments, overstretching the same ligaments by postural strain or injury doubtless has the same effect Arthritic changes in the joints formed by the articular facets have been demonstrated by gross pathologic and histologic examinations of the synovial tissue It is reasonable that pain could originate from these and be referred to the same location as when the corresponding disk is involved

If we accept Doctor Key's hypothesis that degeneration of the disk is the chief cause of backache, his method of treating them by incision and curettage still remains open to question Removal of diseased portions does not necessarily arrest the degenerative process Complete removal of the disk by curettage is virtually impossible, and even if it could be accomplished we do not know that it would stop back pain or even the protrusion of more disk material against the intervertebral ligament Until we

know the causes of degeneration of the disk, we cannot have a logical treatment for preventing or controlling herniation. Certainly, curettage of the unruptured "hidden" disk appears illogical.

Curettage of the disk for relief of back pain should not be regarded as comparable to removal of a disk nodule which is protruding against and compressing a nerve root. The latter has a rational basis, presents a characteristic syndrome that can usually be proved by roentgenographic examination in an opaque medium and the results in well-selected, proved cases are excellent. These probably comprise the majority of the ten per cent of cases to which Doctor Key has referred.

To me, Doctor Key's speculations have been interesting but have added nothing to our real knowledge of the causes of back pain.

DR R. L. RHODES, Augusta, Ga. After the facetious remarks of the previous discussers I rather hesitate to speak, but I feel very strongly upon one point which I offer for your consideration. Down our way we have a man who has done a good deal of work on nutritional problems, as many of you know—Doctor Sydenstricker. Under this stimulus I began the study of these cases from the standpoint of nutrition and have come to the conclusion that many of them do not belong in the realm of surgery but in that of internal medicine—problems of malnutrition and avitaminosis. In many cases a careful history will reveal that they have or have had pains in other nerves of the body, facial, intercostal, *etc.*, in addition to the pain in the back and down the sciatic nerve. Internists are seeing many more cases of neuritis of various nerves than ever before, and lay less stress upon focal infection and more upon malnutrition and avitaminosis as the causative factors.

I have had more than 100 cases, have not operated upon one, or seen occasion to refer one to a neurosurgeon for operation. All are people who have been living upon a high acid-ash diet which not only produces a so-called "acidosis" but is low in some of the vitamins. They have cleared up under a carefully balanced diet chemically, rather to the alkaline-ash side to start with and swinging to a normal balance as improvement occurs, plus large doses of the B-group vitamins, thiamin 50 to 100 mg., nicotinic acid 50 to 100 mg., and riboflavin 5 mg. three times a day, this being reduced as pain and discomfort lessen. A good many of these patients had been advised to have a disk removed and sought other advice before submitting to the operation.

In addition to these, I have had 18 cases who had had disk operations, and who were suffering as much or more than before the operation, several having also one or more other nerves involved. These, also, have cleared up under the measures outlined above, and four of them are now in the armed forces. Therefore I leave this thought—that chemical imbalance of diet and vitamin deficiencies (avitaminosis) are tremendous factors in the solution of many of these problems.

DR W. J. MINTZ, Boston, Mass. It seems that the early work in the intervertebral disk has stirred up a hornets' nest. I cannot go all the way with Doctor Key in his speculations. I feel, when it comes to the question of making a diagnosis of ruptured intervertebral disk, that I must have pretty definite evidence before I will accept the diagnosis. I expect to find a fairly classical syndrome, with sciatica, and I want to have visualization by an opaque material, preferably pantopaque. This is my personal opinion in the matter of making the diagnosis of ruptured intervertebral disk. I have operated upon a considerable number of cases without visualization of a ruptured disk or with negative visualization. Once in a while you will find a definite protrusion; more often you will not. These patients do badly, they come back to haunt you, particularly if you have stirred up a disk that was comparatively normal.

My feeling is that I am only interested in the case that demands surgery, in which I can prove a ruptured disk, and I do not want to make that diagnosis unless I can prove it by a protrusion I can see in the spinal canal following visualization. The other cases I would prefer to leave, temporarily at least, as an unsolved problem.

DR PHILIP WILSON, New York, N. Y. I think Doctor Key must have foreseen that the paper he was to present at this meeting would arouse considerable discussion and it may have been with the idea of obtaining some support that he invited me as a guest. Whatever the motive, however, I am grateful to him for the opportunity to be present.

Doctor Key framed the title of his paper as a challenge. So far as he is concerned, he is convinced that the intervertebral disk is the site of the elusive pathologic changes we have been trying to find in order to understand better this great medical problem of low back pain. He challenges the rest of us to show that he is wrong, I do not believe we can show he is wrong any more than he can prove he is right. Of course, he is excluding from this consideration those cases in which pathologic changes of various types can be demonstrated roentgenologically. But when you have subtracted these cases there still remains a very large group of cases of low back pain. The military hospitals are full of them—young men partly or completely disabled, whose spinal roentgenograms are completely negative. The one new fact added to our knowledge in the last 12 years is an appreciation of the changes, partly degenerative and partly traumatic, that may take place in the intervertebral disks of the lumbar spine. I think if we start from what we have learned in this respect and enlarge and expand the idea a little we will arrive at a position that is not far behind that of Doctor Key.

I will go along with him this far, but I will not agree if the therapeutic implication is to be drawn that the condition is to be treated by direct surgical attack on the injured disk. As a matter of fact Doctor Key more or less skipped the question of treatment, and perhaps he will elucidate more in his closing remarks. We recognize the group of cases with symptoms and signs of intervertebral disk protrusion and agree that a considerable proportion of these require operative treatment, but the remaining cases without evidence of nerve root irritation—and they outnumber the former group by a ratio of at least 50 to one—are in an entirely different class. Many respond favorably to conservative treatment, rest, support and corrective postural exercises. When they do not respond or when they have had so much pain and disability as to require relief from surgery, spinal fusion is the procedure of choice. Immobilization of the damaged joints by an induced bony ankylosis will give complete relief. Most results from these operations have been successful. When pain continues or recurs, a careful check will generally show that the cause is a failure to obtain fusion.

DR FRANK P. STRICKLER, Louisville, Ky. I want to speak on this subject from the standpoint of the patient. We have had a regular epidemic of nucleus pulposus operations in Louisville, and in many cases with very bad results. I, therefore, want to register a plea for conservative treatment of these low back cases. The brakes have to be put on this surgical operation somewhere. In my opinion, far too much surgery has been undertaken on these cases in my locality, and I am convinced that operation was not indicated in a number of these patients, for I have examined about 150 of these patients who have been operated upon and the results were shockingly bad. In fact, such poor results have been obtained that a number of industrial insurance companies in Louisville have refused to have this operation performed upon their patients. There is nothing difficult about the operation and, in some few cases, it is probably indicated. But what about the patient? His symptoms are not relieved, and as soon as he applies for a job and is examined and the classical scar is exposed, he is up against it, no one wants to take a chance on him or his back. So he still has his symptoms and, in addition, has a very difficult time in finding employment.

Let us use some practical common sense before these patients are operated upon, along with observation and painstaking physical examination. This operation is not to be taken casually by either the surgeon or the patient, from the standpoint of after-results.

MAJOR BARNES WOODHALL, Washington, D. C. It may be of some interest to the Association to know something about the results of our treatment of cases of ruptured intervertebral disk in the Army. These statistics were gathered through the kindness of Lt. Col. Michael DeBakey of the Surgeon-General's office. During 1943 the diagnosis of ruptured intervertebral disk was made in approximately 2,450 patients. Because of the line of duty status, or for some other reason, approximately three-fourths of these patients were treated conservatively. By the first of August, 1944, a sample analysis of this group showed that 78 per cent had been discharged from the Army, the assumption being that they could not stand the wear and tear of Army life. A sample of the cases operated upon showed that 31 per cent had been discharged from the Army by August 1, 1944. Among officers, between 0 and 15 per cent were discharged following operation for a protruded disk.

The disposition of patients in the Army depends to a large extent upon man-power requirements. During this period of time we were trying to send men back to even restricted types of duty. I might add that all the patients operated upon had either the classical neurologic picture of a ruptured disk or the lesion was demonstrated by pantopaque myelography. All ruptured disks were visualized at operation and there were no concealed disks.

DR JOSEPH E. J. KING, New York, N. Y. I want to issue a serious warning against making a fad out of this question of herniation of the intervertebral disk. It would be a pity and a catastrophe if the fine work started by Doctor Mixter and Doctor Barr, to whom full credit should be given, should be prostituted. We have had plenty of fads and fancies in connection with low back pain. As all of you may remember, there was a time when, if a patient could be persuaded to lie on the table on his abdomen for a certain period of time, he would get a spinal fusion. This was true especially in certain localities. Fortunately, this kind of teaching has disappeared for we have all seen the bad effects of it.

In recent years, various men seem to assume that practically all low back pain was due to a ruptured disk, and the patient should be operated upon. If this continues there will be many bad results, as has been stated by Doctor Strickler, and people will not be relieved. It goes without saying that in an instance of true herniation of the disk, it should be removed and a good result can be expected in the majority of cases. It is a great pity that men in high position should speak so glibly regarding the association of an herniated disk with any and all forms of low back pain, and I am afraid that when such teaching emanates from high sources, and is disseminated throughout the country, especially down in the smaller communities, many of the younger men will consider the teaching as authentic, and many bad surgical results will follow.

DR J. ALBERT KEY, St. Louis, Mo. (closing) I shall try not to leave anybody out. In answer to Doctor Bennett's remarks, that paper was published in 1924, and I have not published a word on the back since—because I did not know.

In answer to Doctor Magnuson, all the physiologic, anatomic and functional reasons for low back pain and sciatica have been investigated and not until the disk lesions were discovered did we have something we could put our finger on and take out and examine pathologically—and know that this was the cause of the pain.

In answer to Doctor King, orthopedic surgeons have been interested in the disk problem from the beginning. I have not forgotten Joe Barr, and I am sure Doctor Mixter would be the first to admit that he had a lot to do with the discovery of the disk as a cause of low back pain and sciatica. We know that disks degenerate after operation and before operation, and often without any symptoms whatever. Anyone who examines roentgenograms of the low back knows that he sees many films of patients who have objective evidence of degenerative processes in the disks, who give no history of pain in the back or of sciatica.

I agree with Doctor Caldwell that this paper does not add to our knowledge of low back pain, it contains no new discoveries. It merely correlates and rationally interprets facts that have been known for years, which are still being misinterpreted. Treatment is not included in this paper. I do not think the perpetuation of ignorance is going to help treatment. The fact that we now know the cause of the trouble does not mean that we have to subject our patients to operation if they can be relieved by conservative treatment. But we might as well know what we are trying to treat instead of trying to immobilize the spine with the hope that the pain will subside.

Ever since vitamins became fashionable I have given all my patients vitamin B—so much so that they think I have stock in the company—but it does not cure this lesion. This lesion is not due to polyneuritis nor to nutritional deficiency.

Of course we like to avoid stirring up a normal disk and sometimes it is difficult to decide whether the disk is normal or not. If I decide that a given disk is the cause of pain (this is a concealed disk) I take it out. And the more experience I have with this condition, the more apt I am to find something that is the cause of pain. It is fine for the neurosurgeons to say that they do not operate except for the typical syndrome, but they send the patient back to the orthopedic surgeon for treatment. The orthopedic

surgeon holds the bag—and a relatively small percentage of these patients have the typical disk syndrome, but many of them demand relief

In answer to Doctor Wilson's saying that the disk problem is not proved, it is not completely solved, but nothing is proved in surgery if this is not proved. As to the results of spinal fusion, I have reoperated upon five of my own fusions this past summer—and one was not fused—but the pain for which the second operation was performed was due to the disk lesion which I did not find at the first operation, and not to the lack of fusion.

In answer to Doctor Strickler concerning the 150 cases now on his hands who have been made worse by the operation following this epidemic in his city, that must have been very poor surgery, poorly conceived and executed. Everybody knows of some case that has become worse following the operation, but the number is very small. Certainly, in less than five per cent—I would say in less than one per cent—are the symptoms worse after the operation. This would mean that his office is now afflicted with all the failures in about 15,000 operated cases. In my hands the operation is satisfactory in about 85 per cent of the cases. This does not mean that they are all completely relieved, but they are glad they had the operation and so am I. In about 15 per cent they are a good deal better, but not enough to return to their former occupation, and some of these have a good deal of pain. Then there is a very occasional patient (about one per cent) who claims that the disability is worse. I have one case I wish I had never seen, and three or four more that I would just as soon have never seen. With most of them I am very happy.

I did not know that 69 per cent of the enlisted men in the Army with disk operations went back to duty. I think that this is remarkable. I did not know that practically all officers went back to duty. I think the Army is going to reclassify a lot of these backs and use them in light work. This is the answer, just as in civil life.

The history is the important thing in deciding whether or not to operate. What can they do? What will they be able to do after the operation? If they cannot be relieved by conservative treatment and are sufficiently disabled I operate upon them.

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AND

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APPROXIMATELY three years ago to the day, this country was suddenly and furiously plunged into war. Since then many impressive developments have taken place both in the character and progress of the war and in the methods and procedures utilized in its prosecution. Three years of combat experience have stripped us of many encumbering and awkward practices and have provided us with more proficient qualities in waging war. Similarly, in the areas of the war in which we as surgeons are principally concerned, namely, the care of the wounded, combat experience has exerted its inevitably progressive influence. The concentrated experience and the accelerated activity that accompany war permit a more rapid evaluation of the methods and procedures that are applied, and tend to produce early improvements and advances. Measures that prove ineffectual are soon discarded and those found efficacious are just as quickly adopted. This accounts for the changes in concepts and modifications in military surgical practices that have occurred during the past three years of combat experience.

It seems fitting at this time to review, in the light of this and previous experience, some of these developments, to assess the value of procedure adopted, and to indicate the trends in surgical thought on the care of the wounded as obtained from and reflected by all sources available to The Surgeon-General's Office. Proper appraisal of current practice demands comparison with previous experience and, for this reason, it has been deemed desirable to refer wherever it has seemed pertinent to methods and views of previous wars. It is a curious but interesting observation that many of the methods and procedures finally adopted at the close of the last war "had been attempted by surgeons in bygone wars." As emphasized recently by Major General Philip Mitchiner "It is a great pity that our surgeons and would-be surgeons had not acquainted themselves with the Official History of the War of 1914-18 concerning the Medical Services and the principles and practices during that period," for again in this war, as will be shown below, there has been some evident disregard of the experience gained and lessons learned in the last war. As commented previously, learning preferably by immediate and often bitter experience would seem to be not an uncommon human frailty.¹

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SHOCK

Shock has long been considered one of the most serious problems facing the military surgeon, and at the onset of this war great confidence was placed in its therapeutic solution by the development of plasma. Although the development of plasma has undoubtedly been a great contribution, its usefulness in shock therapy can now be viewed in proper perspective. Unfortunately, the early enthusiasm that accompanied this development was so forceful that it pushed aside sound clinical judgment and led to the widespread misconception that plasma could be used as an effective and complete physiologic substitute for whole blood in the management of shock in the seriously wounded. This misconception became so firmly entrenched in the minds of both administrative and professional personnel that it somewhat handicapped the organization and development of more effective measures for the management of shock. With increasing experience in the treatment of shock, it became more and more evident that plasma could not be used as a complete substitute for whole blood. It was found that while seriously wounded men could be brought out of shock with plasma, they were frequently unable to withstand the life-saving surgery that was subsequently necessary. Superficially, such patients appeared ready for surgery, but it was soon realized that this appearance gave a false sense of security for even movement of the patient, anesthesia, and other procedures in preparation for surgery often caused the patient to fall back into shock. It soon became evident that whole blood transfusion was essential for the proper resuscitation of these patients and that whole blood is the only therapeutic agent that will prepare seriously wounded patients to withstand the surgery that is essential for the saving of life and limb. It was further demonstrated that whole blood transfusion at the time of initial treatment will reduce the incidence and morbidity of wound infection during convalescence.

Shock in the great majority of battle casualties is accompanied by considerable loss of blood. The reduced blood volume is due to the loss of both the cellular and the fluid elements of the blood. In such cases, the use of plasma may restore the blood volume but the oxygen-carrying capacity of the circulating blood remains embarrassed. For this reason, the transfusion of whole blood is more effective because it not only supplements the circulating blood volume but it also replenishes its oxygen-carrying capacity. In shock that is accompanied by little or no loss of blood, such as occurs in the early stages of burns, crushing injuries, extreme dehydration, or excessive visceral manipulation, the use of plasma may be considered preferable. Unfortunately, this type of shock is relatively infrequent in warfare.

The great military advantage of plasma lies in the fact that it can be used in situations where the procurement of whole blood is impractical. Its use, under such circumstances, is invaluable for, even in hematogenic shock, it can restore the circulating blood volume and thus, by preventing or reducing the effects of shock, tide the patient over the critical period which may be required for evacuation to a hospital or some other installation where

whole blood is available and life-saving surgery can be performed. Thus, the sobering light of actual experience has delineated more clearly the indications and the rationale of both plasma and whole blood. They are both extremely valuable in the management of shock, but they have their individual and specific purposes and, to be efficacious, must be used accordingly. The change in attitude of Army surgeons toward the use of whole blood can be illustrated by the fact that the present ratio of its use to that of plasma is one to one in contrast to the ratio of one to three in the earlier phases of the war. In the seriously wounded the amounts of whole blood required is even greater than this ratio would indicate. The recent development of the unprecedented program of shipping blood by air from this country directly to our hospitals on the fighting fronts further underlines the importance of whole blood transfusion.

Plasma, of course, was not available in the last war, although its use was suggested.³³ However, the value of whole blood transfusion in the treatment of shock in the seriously wounded was fully recognized. Moreover, whole blood transfusion was employed then in much the same way as now, albeit on a much less extensive scale. Thus, in discussing the problem of providing ample supplies of whole blood for transfusion at the front, it was stated in the British Official History of the last war that "It was felt that if whole blood could be drawn off from donors during times of inactivity and stored ready for use during 'rush' periods, one of the disadvantages of transfusion, namely, the time absorbed in its performance, would be obviated. The giving of blood would then make no more demand on the overworked surgical staff than the giving of a saline infusion." ¹¹ After it has been demonstrated that "Blood, when received into a solution of dextrose and sodium citrate and kept cold could be preserved for several weeks," the principle was tested under war conditions and found satisfactory. In describing the use of this method in the Divisional Area, it was further stated that "A store of preserved blood was kept at the center from which supplies could be drawn for transfusion in the forward area." "This plan of preparing beforehand bottles of citrated blood ready for use was carried out with great success during the heavy fighting in the summer and autumn of 1918."¹¹

There is one other feature of shock that deserves consideration and has perhaps not been sufficiently appreciated. This is concerned with the lethal sequelae of shock. During peacetime shock is observed relatively infrequently and experience with the condition never approaches the massive scale that occurs in war. The lethal sequelae are, therefore, less evident and tend to be less impressive. In war, however, experience with the condition mounts rapidly and attention is directed more forcibly toward these sequelae. Moreover, because of certain conditions imposed by war, wounded men may be in a state of shock with reduced circulating blood volume for a period of hours. The ample use of plasma and whole blood may permit their resuscitation and even the performance of surgical procedures. Despite this, a number of these cases have been observed to die with manifestations of anuria or reduced urinary output. With more effective methods of resuscitation and

improved standards of surgery, these lethal sequelae of shock are becoming more apparent. They may be attributed essentially to asphyxia of organs or tissues during the prolonged period of reduced volume flow of blood. Irreparable damage from shock in such delayed deaths has been demonstrated in the brain, the kidney, and possibly the liver. The urinary suppression in these cases may also be associated with kidney damage resulting from the accumulation and deposition in this organ of liberated hemoglobin or myoglobin in the circulation. Still another factor that may play an important role in the impairment of kidney function in these cases is the presence of sulfonamides. It has not yet been ascertained which of these agents or their combinations is responsible for the serious kidney damage. Field studies are being conducted which, it is hoped, will throw further light on this interesting problem.

WOUND MANAGEMENT

The most common errors in the management of war wounds have been concerned essentially with an inadequate concept of the term "*débridement*," an insufficient realization of the importance of leaving war wounds open or of the proper application of dressings in those left open, and the failure to recognize the need for splitting or bivalving encasements. All of these mistakes were observed in the last war and the essential principles of wound management which have now been finally adopted, at a higher level and on a much greater scale than ever before, were arrived at, perhaps more painfully, in the last war.

Much confusion has arisen about the terms "*débridement*", "*epluchage*", "*parage*", "wound revision", "wound excision", and "wound trimming". There is an apparent need for an adequate expression of just what is meant by each term, particularly as regards the amount of tissue removed. Perhaps some of the confusion has evolved from the difficulty of putting into practice the original and idealistic procedure described, in 1897, by Friedrich, whose aim, on the basis of his experiments, was to remove bacteria from the wound by wide excision of the contaminated tissue in a single mass, such as is done for malignancy. This is a theoretical rather than a practical concept and the physiologically-minded surgeons, who recognize the wisdom of natural processes and know the full meaning of war wounds, find it difficult to accept this procedure as a practicable surgical maneuver. The practically-minded French surgeons have evolved a more realistic and rational procedure and use the term "*débridement*" to describe the opening of the wound¹ by incision in order to expose all recesses, which seems to approximate fairly closely the sense in which the term was originally used by Desault,¹ and by Larrey.¹² The terms "*epluchage*" and "*parage*" refer to the second step of the operation, *i e.*, the removal of contaminated devitalized tissue. As indicated by the terms, "*epluchage*" may be described as a "peeling" of the inner surface of the wound and "*parage*" as a more radical "paring", the distinction is quantitative and relates to the amount of tissue removed. In their effort to abandon the term "excision" and the concept associated with it, the British surgeons in the Mid-

dle East adopted the term "wound trimming." Unfortunately, this has led to further confusion and the misconception that all that was necessary was the removal of loose tags and readily available foreign bodies. Perhaps some have performed the procedure in this manner, but it does not conform with the definition of the operation as "the removal of foreign matter and dead tissue and the relief of tension by incisions planned to facilitate drainage"⁸ It is clear from this definition that at least some British surgeons, like the French surgeons and others who have learned by actual experience, have merely rejected the original idealistic concept that assumes the feasibility of excision of the wound en bloc, and have accepted the more rational and practical procedure of eliminating those local conditions of the wound which contribute to the development of infection. Although some differences may exist as to the actual amount of tissue that should be removed or to the extraction of metallic fragments, there now seems to be fairly general accord among experienced war surgeons on certain principles, all of which became well recognized toward the close of the last war. The first of these is the provision of adequate exposure by incision. The track must be laid open throughout its extent. In most cases, this implies removal of the foreign body, for it is not otherwise possible to expose all recesses of the wound. Under certain circumstances where small shell fragments are unlikely to cause trouble and where their removal would unduly lengthen the operation and endanger the patient, it is perhaps best to leave the foreign body alone. The failure to perform this step in the operation, *i e*, free incision of the wound, is perhaps the most common mistake of the beginner and is often combined with another error, over-excision of the skin. This latter mistake, *i e*, the excessive removal of skin, probably stems from the original conception that included this as a part of the ritual of *débridement* when the wound is subsequently closed by primary suture. It is not only unnecessary when wounds are to be left open, but is actually harmful because it delays healing and increases the difficulties of secondary closure. The second important principle upon which all agree, and which interestingly enough was fully appreciated and emphasized by Botallo in the 16th century,² is the removal of all devitalized tissue in the wound. There may be some difference concerning the extent of this removal. Some, like the British, are more sparing of bruised tissue while others, like the French, who lean towards "*parage*" are perhaps more radical. It would seem from the descriptions given by Colonel E. D. Churchill,⁶ the Surgical Consultant in North Africa and the Mediterranean Theater of Operation, that the procedure advocated and performed by the Americans, at least on that fighting front, is somewhat more radical than the "*épluchage*" of the French or the "wound trimming" of the British, and less radical than the "*parage*" of the French. If the principle of removal of all devitalized tissue is accepted, different usage of terms assumes academic significance only and the extent of the operation becomes a measure of the technical skill and clinical judgment of the surgeon. The third principle upon which there is complete agreement is drainage, *i e*, leaving all war wounds open. Despite constant emphasis and repeated publications, attempts to "get away with" closure are still observed, especially by sur-

geons recently arrived in battle areas. There has also been a tendency to occlude drainage by a tight pack of vaselined gauze rather than merely to keep the sides of the wound apart by loosely placed gauze. In this connection, recent studies indicate that fine-mesh plain gauze is perhaps superior to vaselined gauze, an observation that receives some support from the authors' experience. The fourth and final principle is immobilization, the significance of which was fully recognized by Hunter who stated that "The first and great requisite for the restoration of wounded parts is rest, as it allows that action which is necessary for repair to go on without interruption." Here, too, there may be some divergence of opinion regarding the details of carrying out this principle. The use of plaster encasements has been found most satisfactory for this purpose, but padding and splitting or bivalving the encasement to avoid constriction has been considered essential although their omission have been common errors. The prolonged splinting of war wounds by the closed plaster method as conceived and used by Pirogoff in the Crimean War and by Ollier, Orr and Trueta in subsequent wars is no longer considered satisfactory for the majority of battle casualties. The tendency to veer away from the long-continued closed plaster treatment of war wounds is a natural consequence of the evolution of the more rational philosophy of wound management that places emphasis on early closure and healing through reparative surgery. The closed plaster treatment obviously does not fit into this program of wound management, since early inspection of the wound and efforts directed toward its closure by secondary suture or grafts precludes uninterrupted prolonged encasement. However, in certain types of injuries in which early closure is not feasible, such as in compound fractures, particularly those of the lower leg with large soft-tissue defect and established bone infection, it may still be applied.

Judged by the highest standards of civilian practice, the military environment precludes ideal surgical practice and imposes certain modifications upon the treatment of the wounded. In civilian life, the injured patient is hospitalized and operated upon within a few hours after injury. Since the average patient can remain in the hospital under close observation until his recovery, it is possible to perform a single operation consisting of two phases: first, the débridement or removal of all devitalized tissue, and then the surgical closure of the wound. In military surgery, the ideal conditions of civilian practice rarely exist. The time-lag between wounding and surgical treatment usually far exceeds the period within which "safe" initial closure of the wound is possible. Even were it possible to institute surgery within a few hours after wounding, the necessity for rapid evacuation in the interest of the mobility of the forward units would usually make it dangerous to institute primary closure immediately following initial wound surgery. Although a certain proportion of wounds treated in this manner would heal satisfactorily, it is not possible to know with certainty in which infection will develop. Primary closure enhances the development of life-endangering infection and interruption in the continuity of professional supervision imposed by evacuation precludes its early detection.

For these reasons, it has become a well-established principle of military surgery that wounds shall be left open after the initial débridement. Although the adoption of this rule has been justified as a safeguard against infection, the inevitable consequence has been a heavy penalty in the form of protracted convalescence and the formation of excessive scar tissue. Efforts to obviate these disadvantages have led to the development of a plan of wound management which constitutes, through its extensive application, a significant advance in military surgery.

This plan, so admirably described by Colonel Churchill,⁵ is based upon a concept of wound management that provides the early routine closure by suture of wounds left unsutured at the initial operation. With the widespread use of secondary closure in wound surgery, the treatment of serious wounds has approached the ideal technic possible under nonmilitary conditions, the major differences being that the two phases of a single operation are separated into two distinct operations performed at different echelons of medical care. The initial phase, done in the forward area, is directed toward the prevention of infection and the preparation of the patient for transportation. Proper débridement of the wound minimizes the chances of infection and prepares the way for prompt and successful secondary suture following evacuation. Chemotherapy, as seen in the use of the sulfonamides and penicillin, is of value in reducing the extent and gravity of invasive infection, but it cannot take the place or minimize the importance of good primary surgery.

The next step in the care of the wound under this plan of wound management is the secondary, or what has been termed the reparative phase, usually done after the patient has been transported to a base hospital. If the initial wound operation has been complete, the wound may be closed by suture, usually at the time of the first dressing on or after the fourth day. The proper time for secondary closure by suture is determined by the gross appearance of the wound rather than by bacteriologic studies as was formerly considered necessary. This shift of emphasis from the microscopic to the clinical appraisal of the wound, which cuts across the lengthy arduous laboratory procedure that was previously considered a requisite for secondary suture, is a real advance in itself and is partly responsible for the practicability of secondary wound closure on a large scale. If there is evidence of slight infection, appropriate measures are taken to "clean-up" the wound prior to instituting secondary closure, usually a few days later. If the established infection is severe, or if the patient is toxic or anemic, a course of penicillin therapy and blood transfusion is instituted and followed by surgical revision of the wound and staged closure. The number of soft-part wounds closed in the manner described reach well into the thousands. Good healing has been recorded in from 90 to 95 per cent and no serious complications have been observed. The more complicated types of wounds, such as those involving bones or joints or those manifesting penetration of the viscera, require more elaborate care. In these wounds, there is greater danger of infection and penicillin has been relied upon to prevent infection during both stages of treatment and until the danger of infection is past.

Surgical procedures have been performed in this manner which, it is believed, would not otherwise have been possible. Also of importance in these cases is the recognition of the need for correcting secondary anemia from initial blood loss, for otherwise chronic infection is encouraged and healing delayed. In order to withstand the extensive corrective surgery which many of these patients require, adequate support by means of whole blood transfusion is essential.

Thus, it may be observed that a sound and significant concept in the surgical care of the wounded has been finally developed and now applied on a large scale. Healing is accelerated, restoration of function is hastened, and ultimate disability and deformity are minimized by this plan of wound management. Carried to its full extent, it is a plan that embraces three phases in the surgical treatment of the wounded, primary or initial, secondary or reparative, and tertiary or reconstructive. The first two are performed in the theaters of operation and the third is a function of specialized centers in general hospitals in this country. By properly coordinating these three phases in time and space a closer approach to the ideal methods of wound management within the limits of a military setting is achieved.

While this plan of wound management, through its application on a more extensive scale and at a higher surgical level than ever before and through better integration of its phases, constitutes a real advance in military surgery, it is of interest to review previous experiences along these lines¹⁹⁻²⁸. It would seem that here too there has been some lag in the effort made to utilize, from the last war, the "wisdom purchased at so tremendous a price." The slow, costly, and tedious progress that was made in this direction during the first three years of combat experience in the last war has been vividly portrayed in the British Official History, the pages of which read with greater currency than we are wont to admit.^{3, 10} Eloquent evidence of this is afforded by the unanimous conclusions of the Inter-Allied Surgical Conference held in Paris in 1917, some of which are well worth quoting now.¹⁹

"(1) It is desirable that the organization of the Medical Service should be so directed as to permit of continuity in the supervision of the treatment of the wounded men.

"(2) Rapid transport to one of the casualty clearing stations is essential.

"(3) It is an advantage if each of these units has one or more advanced sections nearer to the firing line, for the reception of patients seriously wounded (such as those suffering from shock, profuse hemorrhage, wounds of the chest, abdomen, *etc.*)

"(4) All wounds of war must be considered to be either contaminated or infected.

"(5) The object of treatment should be

"(a) To prevent development of infection if the wound is still in the stage of contamination, or to procure sterilization if infection has already developed.

"(b) To permit of secondary suture, when sterilization is realized.

"(6) In the primary treatment of the wound, excision of contused and lacerated tissue and the removal of fragments of clothing or foreign bodies must be considered as the rule except in certain cases where the patient cannot be kept under supervision

"(7) When the wound has thus been properly prepared, primary suture may give good results, especially in the case of wounds of the joints. Primary suture is not to be undertaken unless the wound is only of some hours' standing (at the most eight hours), and only when the surgeon can retain the patient under his own observation for 15 days

"(8) If primary suture be not undertaken, secondary suture should be performed when the clinical signs indicate that the wound is surgically sterile

"(9) Several methods for the progressive sterilization of wounds are available, which allow of the routine practice of secondary suture"

These conclusions show a close parallel with recent trend of thought in wound management and towards the end of the last war this parallel appears even more striking. Greater and greater emphasis was placed on the very principles which we now stress. Thus, "in the primary treatment of wounds, it was abundantly shown that if the surgical or mechanical treatment had been sufficient it was practically immaterial what form of antiseptic was employed, or whether the wound was dressed with a solution of soap or simple sterile gauze"¹⁹ As greater improvement in the primary treatment of wounds was achieved, the procedure of secondary suture became more common and "the results given show a record of complete success in from 75 to 90 per cent of the cases"¹⁹ Even Carrel's bacterial count which was regarded as "the most important single element in furthering the progress of secondary suture" was "at a later period discounted and more or less discarded" for "the discovery was made that secondary union could be attained when the wound still contained numerous bacilli"¹⁹ However, opinion on this point had apparently not yet fully crystallized for it is stated that "in spite of the assertion by many surgeons that a clinical inspection was sufficient to determine the suitability of a wound for secondary closure provided constitutional symptoms were absent, it remained a fact that the employment of the bacterial standard insured the largest proportion of successful secondary closures"¹⁹

CHEMOTHERAPY AND WOUND INFECTION

The glowing reports which were based upon and immediately followed the Pearl Harbor experience gave great impetus to the use of sulfonamide therapy as a means of controlling infection in war wounds^{23, 29, 31} As a result of this and other overenthusiastic reports, which were further heightened by the dramatic and publicity-wise efforts of the press and radio to single out sensational achievements, the impression became widespread, both in professional and lay minds that at last an effective antibacterial agent was found and that the great scourge of war wounds, wound infection, could now be adequately combated by merely dusting the wound with sulfonamide and having the soldier swallow a few tablets of the miracle drug. Subsequent developments, and

time, have demonstrated that these early reports were based more upon hope and enthusiastic impressions than upon facts and sober evaluation. In many respects this was unfortunate, for it led to a shift of emphasis, especially in the minds of surgeons inexperienced in traumatic surgery, from the application of well-established surgical principles to the utilization of a simpler and easier substitute. This occurred despite the fact that the early reports which proclaimed the value of the sulfonamides included the need for applying good surgical principles^{23, 29, 31}

Although the exact status of chemotherapy as regards wound infection has not been completely established, sufficient experience has now accumulated to permit certain observations. There is no good evidence to show that sulfonamides used locally, systemically, or combined can appreciably reduce the incidence or gravity of local wound infection or delay its development. In fact, the best controlled studies of this nature, while not applied to war wounds but to wounds far more favorable for demonstrating the possible beneficial action of sulfonamides, have led to the disappointing conclusion that they exert no important influence in combating local wound infection^{21, 30}. Comparable studies on a large scale under a military environment have not been reported, although similar well-controlled observations on war wounds incurred in airmen have been made and the results of these observations show no significant differences between the sulfonamide-treated cases and those in which it was not employed. Summarizing the experience in the North African Theater of Operation, Colonel Churchill⁶ stated that "there has been no conclusive evidence presented that the significance of the time-lag (between wounding and surgical treatment) has been altered by the prophylactic administration of sulfonamides in the field, although this program has now been followed with reasonable precision for a full year." Well-controlled studies have been made on the use of chemotherapy, including penicillin, in the secondary closure of soft-part wounds in which the initial operation has been properly performed and it has been conclusively shown that they contribute nothing to the success of this procedure. Although complete evidence is not available, there is some reason to believe that the systemic use of sulfonamides has been of value in controlling invasive infection and preventing death from sepsis.

Penicillin was introduced on the surgical stage at a time when experience was beginning to fade the spotlight on the sulfonamides and direct it again on good surgical principles. This, together with other reasons, permitted its more cautious and rational application in wound surgery and a more sober and intelligent evaluation of its efficacy than was the case with the sulfonamides. Although its precise value in wound management is yet to be completely established, all the evidence points to the fact that as an adjunct its qualities are far superior to those of the sulfonamides. It would seem to be especially useful in the more complicated wounds in which the danger of infection is greater, such as those with bone or joint involvement and those with penetration of the viscera. At present in these cases penicillin therapy is continued after the initial operation and maintained through the period following subse-

quent surgery until the danger of infection is passed. Based upon his extensive investigations on chemotherapy in battle injuries in the Mediterranean Theater, which have contributed immeasurably to the development of this more rational concept of wound management, Major Champ Lyons states "Local penicillin therapy is used only as a supplement to systemic therapy in the treatment of injuries or infections involving the joints, serous cavities or sub-arachnoid space. No local therapy has been used in other wounds, reliance being placed on *systemic* penicillin to check or abolish *invasive* infection. Anaerobic wound infection is controlled by the excision of dead cellular protein and the avoidance of primary wound closure. Aerobic wound infection is controlled by preventing wound exudation through the use of splints, pressure dressings and the secondary closure of clean wounds. Contamination of wounds with air-borne wound pathogens is decreased by the abandonment of needless changes of dressing. Repeated local applications of antibacterial agents are incompatible with the efforts to prevent wound exudation and the accumulation of dead plasma protein in the wound." Thus, the use of penicillin as provided by this concept of wound management has made possible the earlier and safe application of the extensive corrective surgery that many of these patients require. The experience so far obtained in the use of penicillin in the surgical management of wounds and wound infection has emphasized both its rôle as a valuable adjunct to surgery and the importance of fundamental surgical principles. It is believed that in this way penicillin has broadened the horizon of surgery.

Perhaps the most serious infection in war wounds is gas gangrene, the occurrence and management of which may be regarded as one index of surgical accomplishment and of the success of other measures in the care of the wounded. In the last war the incidence among our troops was 1.7 per cent. Unfortunately, no precise picture of World War II incidence can be drawn at this time. However, the fragmentary incidence points to the likelihood that the current experience is only slightly more favorable than that of World War I. Until quite recently, and except in selected groups of cases, there has been no evidence of any considerable reduction in the mortality or morbidity attending the infection, the reported experience suggesting a fatality of about 45 per cent in comparison with 47 per cent in World War I.¹⁰ The British experience has been little different, and was aptly expressed by MacLennan who found, on the basis of his observations in the Middle East among British troops, that "neither in prevention nor treatment has much advance been made in the last 25 years" despite the fact that in this period "the potency of antiseptics has at least been doubled and the whole group of sulfonamide drugs introduced."

Properly executed, prompt initial surgery is still by all odds the most effective prophylactic measure and this factor has always loomed prominent wherever there is recorded an appreciable reduction in incidence, morbidity or mortality. Delay in evacuation and in the institution of surgery or the performance of inadequate surgery has been observed to foster the development

of the infection in wounds received in this war, as in the last war. Although efforts have been made to produce an agent capable of immunizing against the infection, this development has not yet reached the final stage of practical application. Sulfonamides have not proved effective in either the prevention or the treatment of the condition and there is no evidence to show that antitoxin is especially valuable. Penicillin, which offered real promise experimentally, is yet to be thoroughly evaluated. Tentatively, it may be stated that there is little likelihood that it would be effective prophylactically since the infection has occurred in patients who were receiving adequate prophylactic therapy. This has theoretical approval since the drug cannot reach devitalized tissue. On a similar basis, its therapeutic rôle should be in limiting the extension of the infection, a belief which gains support from available clinical experience.

Thus, it may be observed that in the management of wounds and wound infections emphasis has again shifted back to the importance of fundamental surgical principles and the rôle of chemotherapy remains a supplemental one. Here, too, we find a striking parallel with the experience of the last war, during which "early efforts to control the infection of wounds relied mainly on the use of chemical antiseptic application"—and the numbers tried were legion. Only toward the end of that war was it fully appreciated that "the mechanical ablation of the contaminated or infected tissue was the single effective factor." Following a consideration of chemical media employed in wounds at that time it was concluded that the "supporters of antiseptics gained the initial success, but it was by the odd paradox that the success of the antiseptics depended upon the skill with which the surgical means forming a part of the system was perfected and carried out. Even enthusiastic supporters of the antiseptic system discovered that in a wound treated by exposure to the sun, the same mathematical estimate of the length of time necessary for its closure could be made as with the Carrel-Dakin system, and that the period necessary was practically the same in both cases."¹⁹ The almost inherent urge to place some agent, with hopeful healing and anti-infective properties, in a wound seems to lie deep-seated in the human breast and is as difficult to control as the better recognized human impulses. Time and experience have repeatedly demonstrated the inefficacy of such agents. Perhaps some day such an agent will be found but the search seems futile when it is realized that the key to wound infection in traumatic wounds is dead tissue, a fact which Botallo recognized almost four centuries ago, and which Lister fully appreciated.

MAXILLOFACIAL SURGERY

The following statement which was made in the Medical Department, U. S. Army, History of the World War, applies equally well to maxillofacial surgery in the current war. "Very few new principles as regards maxillofacial surgery were developed during the war but the large number of wounds of this character encountered as compared to their frequency in civil life

afforded unprecedented opportunity for demonstrating the advantages and faults of the various operative procedures which had been devised"²⁰ In fact, as one reads further of the management of maxillofacial wounds in World War I, one is struck with the fact that nearly all the presently recognized fundamental principles were advocated at that time. These are, in brief, the conservation of all viable tissue, the early reduction and fixation of skeletal injuries and the suture of soft-tissue where this is possible without undue tension, the establishment of provisions for adequate drainage and the maintenance of moist pressure dressing, and provision for adequate respiratory airway (by means of tracheotomy if this seems necessary). As experience in this war has accumulated, the importance of these principles has been further emphasized.

NEUROSURGERY

The technic of the management of cranial wounds, as developed by Harvey Cushing in World War I, remains today as the one of choice. However, in the subsequent repair of skull defects which are an inevitable consequence of many of these injuries, a distinct advance has been made in this war with the use of tantalum plate.

With the widespread emphasis placed upon prompt secondary closure of wounds, an earlier opportunity is being afforded for the suture of wounds of major nerves than ever before. In the first months of the war, all cases with nerve injuries were returned to this country for suture, whereas now in many instances nerve suture is being performed in general hospitals abroad with a consequent saving of vitally important recovery time. Experience has proven the value of a sling suture of fine wire between the nerve ends in cases where, during the initial wound revision, it was impossible to accomplish end-to-end suture. This prevents retraction of the cut ends of the nerve and, likewise, permits their easy identification at subsequent operation.

The most approved method of suturing nerves at present is with fine tantalum wire on atraumatic needles followed by wrapping the line of anastomosis with tantalum foil. The latter prevents the nerve from being engulfed in scar tissue and serves as a guide for the down-growing axis cylinders. Until more time has elapsed, a proper evaluation of the results being obtained in nerve suture in this war cannot be made. In an effort to follow these cases for a sufficient period of time to determine the end-result, the Army has issued directives that such cases must report for periodic examinations every three months until the maximum hospital benefit has been accomplished, and has established a Nerve Registry in the Office of The Surgeon-General for all these cases.

THORACIC SURGERY

Owing to the oft-repeated dictum "Sucking wounds of the chest must be closed at once," attempts were made in the early days of the war to suture such wounds hastily when they were first seen, and often under

conditions which were far from ideal. As a result, many of these wounds broke down, resulting again in a sucking wound which could not be re-sutured due to the surrounding infection. Experience has shown that until the casualty has reached a hospital where adequate facilities exist for careful preoperative preparation and for painstaking surgery, sucking wounds should not be sutured, but should be closed promptly by means of a pad of vaselined gauze molded to fit the opening in the thorax over which a tight adhesive dressing is applied. It is interesting to note that Yates advocated this same procedure in the last war for the same reasons. Another reason for not performing immediate definitive surgery in the case of patients having serious thoracic wounds is that experience has shown they must be brought into a state of equilibrium before they can tolerate major operative procedures. This means that these patients need blood, warmth, rest, freedom from pain and time for readjustment to the changed physiology of respiration if they are to have the best chances of surviving operation.

As the war has progressed, there has been a decided shift to early aspiration of hemothorax in contrast to the feeling in the earlier phases of the war that aspiration should be delayed for several days. The principle of delayed aspiration was based on civilian experience with stab wounds and bullet wounds of the thorax without much soft-tissue or lung damage, and on the theory that the blood in the thorax acted as a deterrent to further bleeding from the lung. In the case of war wounds, in which there was considerable damage to the thorax and in which foreign bodies such as bits of clothing and rib fragments were complicating factors, infection has been found to be frequent. Delayed aspiration, therefore, resulted in many cases of infected hemothorax, in which the entire pleural cavity was involved. It has been discovered that bleeding from the lung does not recur with early aspiration and that the presence of blood in the thorax does not prevent bleeding from the chest wall. The advantages of early aspiration are stated to be that

- 1 It relieves high intrapleural pressure
- 2 It removes an excellent culture medium for bacterial growth
- 3 It aids in early expansion of the lung—a definite advantage in limiting the area of empyema if infection occurs
- 4 It decreases the incidence of massive clotting
- 5 It prevents the late fixation and contraction of the thorax

The present procedure of choice is aspiration of all the blood from the thorax within the first 24 hours and daily repeated aspiration if necessary to keep the thorax free of blood. The use of air replacement after aspiration of the thorax which was advocated in the early phases of the war has been abandoned for reasons previously presented⁴. In the light of present experience, the severe criticism of air replacement therapy by members of the American Medical Unit detailed to the study and treatment of thoracic injuries during World War I is of interest³⁴.

Probably the greatest advance in thoracic surgery in this war has been

in the management of cases of massive clotting of blood in the pleural cavity and of empyema. Massive clotting of blood in the pleural cavity occurs in about four to six per cent of cases with hemothorax and should be suspected when clinical findings persist after only small amounts of blood can be withdrawn and serial roentgenograms show no improvement during the third to sixth weeks. Using penicillin therapy as an adjunct early operation is done in these cases with removal of clots from the pleural cavity and the dense layer of fibrin from the underlying lung in order to permit rapid expansion of the lung and thus obliterate the cavity. Similarly, in post-traumatic empyema if extensive collapse of the lung occurs early surgical decortication is performed. The application of these surgical principles and this shift of emphasis from local treatment of secondary pleural complications to procurement of early and complete reexpansion of the lung has provided a significant advance in the management of these serious injuries.

PENETRATING WOUNDS OF THE ABDOMEN

A striking reduction in mortality in cases of penetrating wounds of the abdomen has been accomplished in the present war. In World War I, the mortality among such cases which reached the forward hospitals was 45 per cent, whereas the most accurate figures that can be assembled to date in this war indicate a mortality of 15 to 20 per cent in similar groups of cases. This lowering of mortality is apparently due to three main causes:

(1) Use of ample amounts of whole blood both in the preparation of these cases for operation and during and after the operative procedure.

(2) The availability of larger numbers of well-trained surgeons far forward in the combat areas in installations in which careful surgery can be done and good postoperative care continued.

(3) The widespread use of exteriorization of wounds of the large bowel and of colostomy in the management of these wounds and those of the rectum.

Exteriorization of the damaged segment of bowel through a laterally placed muscle-splitting incision is at present the procedure of choice in the management of wounds of the colon. When exteriorization is not possible, the perforations must be repaired by sutures and a proximal colostomy established. In cases of perforation of the rectum, colostomy is mandatory, and in addition, free posterior drainage of the wounded segment of rectum must be accomplished. This is best established by incision of the fascia propria with exposure of the rectal, sacral, and lateral paramedian spaces.

Two types of colostomy may be performed at the initial operation.

A Loop Colostomy. The bowel is so mobilized that the exteriorized segment will lie on the abdominal wall without tension. No sutures or clamps should be used to fix the bowel in place. This type of colostomy is especially indicated in perforations which do not involve more than one-half of the bowel, and as a proximal sigmoid colostomy in cases of wounds of the rectosigmoid or rectum.

B Spur Colostomy In the formation of a spur colostomy, the bowel must be mobilized so as to afford free ends at least six inches in length. These are joined by two rows of catgut sutures, preferably placed along the longitudinal fascial bands. This type of colostomy is indicated where perforations are larger than one-half the diameter of the bowel, in injuries which require resection of a portion of the bowel, and in complete transection of the gut.

Colostomy was employed in some of these wounds in World War I, but its use was not considered of the unusual value which is attributed to it today. The following statements from the History of World War I are of interest in this connection: "Colostomy is to be advised in large ragged openings, particularly those occurring in the cecum, descending colon, and sigmoid." "The wounds that are sutured do better than those in which an artificial anus is employed, the latter group gives the high mortality rate of 70 per cent."¹⁸

The vertical paramedian incision has been found to be the one of choice and the least liable to complications. Closure of celiotomy wounds with rows of buried sutures has been abandoned by many military surgeons of wide experience since it has been considered to contribute to deep infection of the wound. The most widely accepted method of closure consists of the use of a continuous absorbable suture for the peritoneum followed by interrupted stay-sutures of wire or heavy silk. The skin and subcutaneous tissues are not closed, but are separated by a strip of vaselined gauze.

BONE AND JOINT SURGERY

In general, it may be stated that among those surgeons who have had a wide experience with gunshot fractures of the long bones, the trend is distinctly away from "salting" these patients away in plaster encasements and leaving them there until the odor demands a change of the encasement. Under this regimen, the wound will heal in due time, but at the costly price of muscle atrophy, joint fixation, and even skeletal deformity. Efforts to obviate these disadvantages have led to the development of a more active program. At present, the management of a case of gunshot wound of the thigh with fracture of the femur consists of adequate débridement in a forward hospital, secondary closure of the wound in 4 to 12 days in a base hospital, followed by the application of skeletal traction with restoration of length and alignment, maintenance of this traction until the fracture has partially consolidated, application of a plaster encasement for evacuation to the United States, and removal of the encasement on arrival here, with application of suspension traction until firm union permits ambulation with crutches. With this method of treatment, the soft-tissue wound is healed in two weeks, there is little atrophy of important muscles, the joints are kept mobile and union with good length and alignment is achieved. This is in striking contrast with the patients who were received in the hospitals in this country in the earlier days of the war, and had been treated by the "salting down in an encasement

method" and whose wounds were still draining pus, whose bone position was far from ideal, whose joints were stiff, and whose muscles were atrophied

It has been found advisable to operate upon cases with joint wounds promptly, at which time the joint is opened widely and all loose cartilage, bone and foreign bodies removed. The joint is filled with penicillin solution and the synovial membrane closed, leaving the skin open for subsequent secondary closure. Even if initial operation is delayed for a day or so, this method of treatment is advocated unless there is a fulminant infection present. External skeletal fixation has not proven practicable in combat areas, and its use has been restricted to hospitals in the rear and to those cases with loss of bone substance or with fractures not reducible in the usual fashion.

BURNS

At the beginning of the war, the lack of uniformity of opinion concerning the proper local treatment of burns was evident from the varied types of treatment which were advocated at that time. The most popular of these was the use of tannic acid, while others, such as triple dye films of various materials and even paraffin had their stout supporters. Largely due to the results obtained by its use in the Coconut Grove disaster, the pressure dressing applied over fine-mesh vaselined gauze emerged as the method to be adopted by the Army, and the use of tannic acid by Army surgeons in the treatment of burns was forbidden. This pressure dressing method which had been so strongly advocated by Koch has proven eminently satisfactory in the Army. This, together with the fact that the incidence of burns in modern warfare has been less than originally anticipated, has made the problem of burns less significant.

CONCLUSIONS

Finally, it is evident from this brief consideration of approximately three years of combat experience that definite progress has been made in the surgical care of the wounded. This is clearly reflected by the results that have been achieved, for there can be no question that the survival rate among our battle wounded is higher now and the morbidity rate lower than ever before in the history of warfare. While there are undoubtedly many factors that have contributed to this gratifying achievement a critical review of the past three years of combat experience throws into bold relief the one factor that has contributed most—the high standard of surgery being done. At the applied level of practice, this standard of surgery is higher now than ever before, primarily because of the greater availability of formally-trained and well-qualified young surgeons and because of their placement by the organization and plan of medical service, where their skill and talent can be utilized most effectively in the early as well as the subsequent care of the wounded.

It must be acknowledged, however, that while definite progress has been made, it has occurred at the expense of some retardation earlier in the war through repetition of some of the mistakes made and lessons learned in

the last war To some extent, this may have been due to the fact that the most significant surgical thoughts which emerged from the experience of the last war were just beginning to crystallize when the war ended, with the result that much of their lasting value was lost The fact, too, that the publication of the last war's medical history was considerably delayed, and did not appear until after all interest in military surgery had waned to the point of cheerfully relegating these tomes to archival desuetude, may have been a contributing factor in this connection Thus, all the experience of the past three years in the management of war wounds has again affirmed the importance of the fundamental principles of good surgery, principles which became well recognized toward the close of the last war and which critically-minded surgeons have long espoused At our disposal now are more effective measures of resuscitation and superior agents for the control of infection, but experience has also shown that they must be considered as adjuncts to, not substitutes for, good surgery They have not lessened the importance of fundamental surgical principles but rather have extended the scope of their application Combined intelligently, these therapeutic adjuncts and basic surgical principles have led to the development of a more rational and effective program of wound management that has already provided the most gratifying results yet achieved in military surgery and gives promise of far-reaching significance This development, which has been realized largely through the vision and efforts of our Surgical Consultant in the Mediterranean Theater of Operation and the sound investigations of his staff, constitutes the major advance in the surgery of this war and points the way to further progress

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REMARKS ON A FEW SURGICAL PROBLEMS IN AVIATION MEDICINE*

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AVIATION MEDICINE is concerned with the medical problems arising from the use of aircraft in flight and, in time of war, those of a surgical nature are greatly increased in number and importance. The character of these problems definitely varies with the hazards involved in the use of the aircraft. That these hazards are increased many fold during wartime flight operations is evident^{1, 2}. Because of the large number of injuries in Air Force personnel engaged in training and conflict, special consideration is now being given to the etiology, treatment and prevention of these casualties. It has been learned that unusual and characteristic wounds may be inflicted by accidents associated with flight. This is not surprising when the extreme forces involved are considered, forces that the human body, used to a different pace and environment, is often structurally unsuited to withstand.

For facility of discussion the casualties are grouped according to their causative factor. These factors are *aircraft accidents*, *enemy gunfire*, *parachute injuries* and *environment*.

CASUALTIES DUE TO AIRCRAFT ACCIDENTS

Aircraft accidents, viewed casually, seemingly result in such severe trauma that what the physician has to offer, either prophylactically or for curative purposes, appears totally inadequate. A more hopeful outlook is obtained when the situation is reviewed in its separate aspects.

As the speed of flight and landing of aircraft has increased, pilot loss from accidents has increased. Tremendous force may be exerted momentarily while velocity changes are occurring. The rate and method of deceleration determine the distribution of this force in time and space. When exerted on a human being the force may be kept below the minimum consistent with life by a small increase in time—space distribution.

As an example—a plane free-falling, without power, reaches a velocity of ± 120 miles per hour. If the plane strikes the ground vertically so that it is stopped after going into the ground six inches, a pilot weighing 150 pounds will exert a force 484 times the force of gravity, or 140,000 pounds, for the period of deceleration. If the plane plows along the ground for 20 feet before it is stopped, the 150-pound man exerts a force of only 24 times his weight, or 3,600 pounds during the interval. This is compatible with life if distributed over a large body surface.

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Another factor in determining the outcome of an airplane crash is the direction of the applied force. If in the vertical axis, from head to foot, the results may be very different from the deceleration force applied transversely to this axis.

DeHaven^{3, 4} has presented factual data derived from persons falling from known heights and terminating their falls by contact with known objects, which indicates that a human being can survive deceleration pressure forces up to 200 times that of gravity, provided it is applied transversely to the long axis of the body and over a large body surface. Much less force can be survived when it is applied parallel to the long axis. The skeletal structures have only a limited space for internal deceleration unless fractured. The internal organs, however, continue in the path of flight after the skeletal structures are arrested. They are eventually stopped by their vascular and ligamentous attachments, but if the force is too great these may be severed, in which case only the confines of the somatic cavity retains them. The path through which the internal organs may move under these circumstances is longer in the longitudinal than in the transverse direction and the potentialities for damage are much greater.

Hass⁵ has accurately described the pathology encountered in pilots who have died from forces exerted upon them during airplane accidents. The difference in the rate of deceleration of the skeleton and its contained viscera results in lesions that vary from minor lacerations of one coat of an organ to complete tears of the entire structure. No organ escapes, but the more mobile and bulky are the first to be damaged. The heart, aorta and lungs may be involved with hemorrhage from tears in the auricles, pericardium, pleuropericardial junction, aorta, and parenchyma of lungs. Pulmonary emphysema is common. Lesions below the diaphragm result in wide, gaping lacerations of the liver and spleen, with the latter partially to completely pulled from its pedicle. The small intestine, especially the ileum, may be stripped from its mesentery or actually ruptured.

Clinically, sublethal damage, unless anticipated and recognized, may readily progress to a stage incompatible with life. To be recognized are hemopericardium, cardiac tamponade, pneumothorax, hemopneumothorax, intrapulmonary hemorrhage, diaphragmatic, liver, splenic and intestinal rupture, or mesenteric evulsion of the small intestine,⁶ and fractures of all types. Knowledge that such lesions may exist and can be present without evidence of external body trauma will lead to a search for them clinically.

Impact of portions of the body against protruding objects in the plane or on the ground result in puncture wounds, evulsions of tissues, fractures and maxillofacial injuries. The treatment in no wise differs from the care of these conditions caused from any other means.

Hot motors and incendiary missiles contacting spilled gasoline cause frequent fires in plane crashes. These result in burns varying from the superficial flash type to complete incineration. The flash burns are usually of the face and hands, as the remainder of the body surface is covered by the aviator's

clothing The intense fire from gasoline will quickly consume an unconscious pilot, and in such instances only a charred torso may remain

CASUALTIES DUE TO ENEMY GUNFIRE

The missiles from enemy gunfire causing casualties in the Army Air Force combat crews are 20-Mm cannon shell, machine gun bullets, both 7- and 13-Mm, anti-aircraft cannon shell, rockets and secondary missiles from the plane structures

The characteristics of these wounds depend upon the conditions under which they are produced The wall of the airplane must be traversed by the missile before the flyer is struck in the majority of instances Thus, a bullet which ordinarily would be going forward, end-on, may be caused to tumble in its flight There is a great difference in the physical aspects of the two wounds

The "end-on" bullet, traversing soft tissue, produces a clean wound, with a small entrance and exit and a small channel through the tissues Tumbling (yaw) produces enormous, destructive wounds The entrance wound is only moderately enlarged but the exit wound is "explosive," and is many times larger than the hole of entrance The channel is funnel-shaped, with the large opening toward the point of egress of the bullet The size and character of a wound are dependent upon the amount of energy that the missile producing it expends on the tissues in passing through Therefore, the increased resistance that is offered to the passage of a bullet turned partially sidewise accounts for the production of the larger wound If bone is struck by either type of bullet, its shattered fragments will, by the momentum imparted to them, produce secondary damage to the soft tissue

A shrapnel wound is similar to that produced by a tumbled bullet Not infrequently, because of its lesser velocity or greater presenting surface, it may not possess enough energy to force it all the way through the tissues In that case the wound of entrance would be the large end of the cone

A 20-Mm cannon generally produces wounds similar to anti-aircraft cannon (shrapnel) but smaller in size, provided the shell has been exploded by contact with the plane structures or body armour If it is exploded by direct contact with the body, the resulting wound may be enormously destructive

In general, it may be said that the size and character of a wound imparted by missiles from gunfire depend upon the velocity, mass and presenting surface area of the fragment, and the resistance offered to its passage by the tissues involved

CASUALTIES DUE TO PARACHUTE INJURIES

Injuries associated with parachute escapes from combat planes are very frequent in contrast to those associated with the parachute jumps of the paratroopers Approximately 37 per cent of all who are forced to take such a means of emergency exit from an aircraft suffer death or some disability

A special study by the Medical Safety Division, Office of Flying Safety of the A A F, revealed that four emergency parachute jumps were made daily by some Air Force member in the continental U S A and of these, one was injured each day and one killed every other day⁹

At the present time, one out of every eight emergency parachute jumps ends fatally Of the escapes which end in fatalities, 48 per cent jumped from

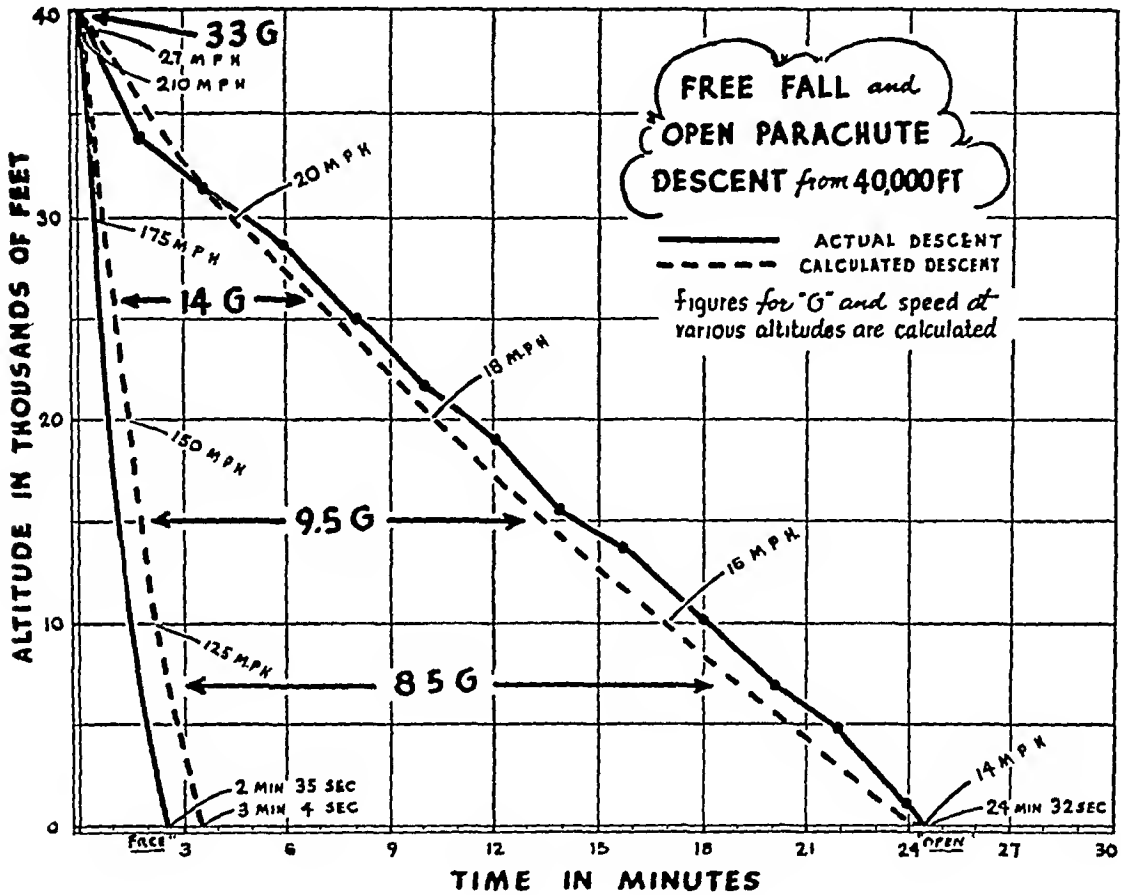


CHART 1 —Diagram showing speeds of free fall and open parachute descents from 40,000 feet of a 200 pound man
Note The force exerted on a free falling parachutist when his parachute is opened, varies according to the altitude This force is shown in "G's" which are multiples of the pull of gravity, one "G" being the normal weight of the individual

too low an altitude, 20 per cent hit the aircraft on bailing out, 10 per cent had their chutes fouled on the aircraft, and 22 per cent were killed from miscellaneous causes

One out of every four persons who uses a parachute for escape purposes is nonfatally injured Ninety per cent of the injuries are incurred on landing

There is a wide variation in the amount of force exerted upon an individual when a parachute is opened during a free-fall at different speeds and altitudes (Chart 1) The variation is also noted between individuals checked by parachutes at the same height due to differences in position, surface exposed, streamlining and weight of the falling mass Examples will be given to illustrate, using average figures At 7,000 ft altitude the force exerted in retarding the fall of a 200-pound man on opening his

"chute" is equivalent to 8.5 times the force of gravity ($8.5G^*$). This rapidly increases with the higher altitudes, and at 40,000 ft the force necessary to do the same work is $33G$. Expressed in practical terms, the chute at the moment it is opened must be able to support an applied weight of 33 times 200 pounds, or 6,600 pounds. A body falling free through the atmospheric pressure encountered at this altitude will travel at approximately 210 miles per hour. If the plane is going 400 miles per hour, the necessity for allowing a definite time-lapse to occur between bailing out and the opening of the chute becomes apparent. This will permit deceleration to the free-falling speed. Of course, the lower the altitude the greater will be the difference in rate between the top speed of a plane and the terminal velocity of a free-falling body.

If the chute is opened before the body of the jumper has lost the speed of the plane, the chute may be torn from the shroud lines, at the same time inflicting severe damage on its occupant. One such injury has been known to sever the legs from the flyer's torso. Others of less severity have resulted in fractures of the vertebra, rupture of the diaphragm and rupture of the jejunum.⁶

CASUALTIES DUE TO ENVIRONMENT

Frostbite —The environment of high altitude flights exposes the aviator to extremes of low atmospheric pressure, low temperatures and low oxygen concentration. The two latter conditions, with the added factor of exposure, result in the clinical manifestations of so-called "high altitude frostbite."

The lowered temperatures, often $-50^{\circ}C$ at an altitude of 35,000 ft, result in rapid severe freezing when a part of the body is inadvertently exposed, even for a brief period. The anoxia that a flyer is prone to develop at high altitudes facilitates the freezing. In the early part of the war a large part of all the AAF combat casualties in the European Theater were due to this type of frostbite. This number has been greatly decreased during the past year by studious redesigning of planes, more appropriate clothing, electric heating of gloves and flying suits and education of the flying personnel.

The clinical manifestations depend upon the severity of the freezing that has occurred. Mild frostbite may result in weeks or even months of hypersensitivity to temperature changes. Severe frostbite may result in permanent disability and occasionally loss of an extremity. The toes, fingers, ears, nose, cheeks and forehead are most frequently involved. The relative susceptibility of these parts to frostbite is variable.

Only certain features of the pathologic physiology are definitely understood. An attractive theory, elaborated by Loyal Davis, and his coworkers,¹⁰ would indicate that an initial reflex vasospasm of peripheral arterioles, with resultant ischemia, occurs in the exposed part. Following this, the vasoconstriction at the terminal end of the arteriole may persist for varying lengths of time, up to 24 hours, or longer. Microscopic examination of the capillary bed of the finger tips at this time reveals that the peripheral ends of the

* " G " = the normal weight of the individual

arterioles are well filled with blood, but that the terminal capillary loops are empty. In instances where the exposure is less severe, the capillary circulation is reestablished, with damage only to the endothelium. In the prolonged, or extreme, instances of freezing, the arteriocapillary junction becomes obstructed by a thrombus or cellular agglutination, and destruction of the capillary results. Clinically, we may usually differentiate these two degrees of extreme frostbite. In the former, if the vasoconstriction of the arterioles is relieved before obstruction of the lumen takes place and the capillary circulation is reestablished, extravasation of plasma or whole blood may occur through the damaged capillary wall into the tissues. The fluid accumulates as vesicles or edema, and eventually separates the epidermis and dermis at the germinal layer of cells, with desquamation. If a complete mechanical occlusion has developed within the arterioles at their junction with the capillaries before the vasospasm is relieved, no fluid is lost and the "dry type" of frostbite is obtained.

The same pathologic alterations in physiology occur when the frostbite extends to the tissue below the fascia. Capillary damage results in extravasation and hemorrhage into the muscle, while capillary obliteration by obstruction of the arterioles results in dry gangrene. It is evident that the "wet type" is less likely to result in gangrene and loss of the affected part. Circulatory impairment may persist for months or be permanent, leaving a condition similar to endarteritis obliterans, with hyperplasia of the intima of the arterioles.

Other Conditions—Other clinical conditions which are influenced in their production by environmental factors are aero-otitis media and aerosinusitis. The mechanism of production, clinical manifestations and various aspects of treatment are problems of more immediate concern to the Otolaryngologist, and, although pertinent, will not be discussed in this communication.

Lightning is a factor which has caused casualties in landed planes improperly grounded, but there is no recorded instance of this occurring in flight.

AIR EVACUATION OF CASUALTIES

The air evacuation of casualties has been one of the major developments in the transportation of the wounded during this War, accomplishing their swift and comfortable delivery to a hospital equipped for definitive surgical care in the briefest possible time.

This subject, in all its ramifications, is one of great importance when we consider that approximately one-half million sick and wounded have been evacuated by air since Pearl Harbor. From June to October, 1944, 55,000 patients were evacuated from France, with the loss of only four-tenths of one per cent of this number after admission to Army General Hospitals in England.

The advantage in logistics alone recommends this mode of evacuation. For instance, fourteen C-54's (large, four-motored cargo planes), each equipped

with 24 litters, can do the job of six 500-bed hospital ships in carrying patients from the Southwest Pacific. Patient travel time is cut from 24 days to 39 hours, the total crew and medical personnel requirements are reduced from 2,136 for the ships to 336, a much smaller holding hospital is required overseas, and the C-54's can also carry military cargo on the outward trip^{11, 12}

TREATMENT

The details of therapy for each condition of a surgical nature encountered in aviation medicine does not belong to the scope of this presentation. General methods, new advances and consideration of therapy peculiar to Air Corps injuries will only be discussed.

In administering first aid, particular care should be exercised if the tourniquet is used. At high altitudes death of a part from circulatory impairment may be much more rapid than at sea level, due to the state of anoxia initially present. The Gallagher¹³ pressure dressing is now being used in many combat planes to supplant the tourniquet. When this dressing proves adequate in controlling hemorrhage in a wound containing a severed vessel, there is definitely less likelihood of the loss of the extremity.

Shock is a factor in most traumatic wounds. Extremes in oxygen deprivation and lowered temperatures as found at high altitudes augment the development and continuation of this shock. If not destroyed in combat, mechanical means to overcome both of these have been provided in our bombers. The B L B oxygen mask and the demand oxygen system can deliver 100 per cent oxygen. An electric blanket for protection of wounded from the cold is now standard equipment for the high altitude bombing missions.

The primary closure of wounds has been looked upon with disfavor in this war. This has proven sound policy in the care of injured ground troops when the clothes, missiles and body itself may be grossly contaminated by soil. There are a number of factors that tend to reduce the hazard of infection in wounds produced in the air. As enumerated by McFee,⁷ they are

1 Bomber crews are generally in good physical condition. Fatigue and debility are usually at a minimum as the men have been well housed and well fed.

2 A minimum of contamination is present in wounds produced on a flight. The men's clothes and bodies are clean. The missiles are not soiled and the wounds are free of dirt and other material from the earth.

3 Treatment is generally speedily obtained. First aid, including sulfanilamides and blood plasma are administered in the plane. Definitive surgical care during the "golden period"—four to eight hours after injury—is available on return to the air field. This is compared to the treatment of ground troops who, in many instances may have to wait hours and even days for such care.

These factors give a marked advantage in the treatment of air crew injuries. Because of these it should be possible to decrease the immediate morbidity and mortality, as well as the final disability, since factors that dictate against primary closure of wounds are frequently of less importance in these casualties. Advantage should be taken of this when possible.

It has been found useful to give prophylactic doses of penicillin in severely injured casualties, especially those that are so profoundly shocked that débridement and repair of wounds must be delayed. As an example, a severely shocked crash victim was given 100,000 units of penicillin intravenously along with 1500 cc of blood and plasma as an initial procedure in treatment. The injured flier had crashed in a swamp and had been pinned under his plane by a tree for about four hours. The large avulsed wounds of his face and arms were filled with swamp water and tree bark. The wounds were débrided and an additional 100,000 units of penicillin were instilled before they were closed. Each 24 hours thereafter he was given an additional 200,000 units for four days. The wounds healed *per primam*, without evidence of infection.

Little new in the treatment of burns has been devised during the present war, however, progress has been made in the standardization and rationalization of such treatment based on our previous knowledge. Never before has there been as universal an acceptance of one method of therapy. As with the majority of good procedures, the regimen accepted is simple, logical and physiologic. Adequate amounts of plasma and whole blood are available for the primary treatment of the burned, shocked patient. Eschar-forming drugs have been almost universally abandoned.⁷ In their place have been substituted careful, minimal débridement under aseptic precautions, a bland ointment or petrolatum gauze and a pressure dressing. A method to hasten the separation of necrotic tissue has recently been announced.⁸

There is much controversy about the proper method of treating acute frostbite. In various countries diametrically opposed therapy is often used. Regardless of the methods employed, there are certain principles that should be followed. Every precaution to prevent infection must be taken. The vasoconstriction should be relieved before the capillary is irreparably damaged if possible. Some observers believe this may be accomplished by the immediate blocking of the sympathetic nerves with novocaine. At the same time it is desirable to control the edema and vesication of the affected part, as the circulation can be secondarily retarded by increased interstitial pressures. An adequate means of decreasing the capillary permeability has not been evolved, but moderate pressure dressings, aseptic drainage of accumulated fluid and avoidance of excessive heat or cold aid materially to shorten the wet phase. Oxygen therapy is a logical "must" in the acute stage.

Treatment during the chronic period of frostbite includes late amputation of useless parts, skin grafting, physiotherapy similar to that employed in chronic vascular diseases, and temporary or permanent blocking of sympathetic nerves to the involved part.

CONCLUSION

In the future, many lives will be saved by the development of means of preventing casualties from the forces encountered in flying. These de-

velopments will include redesigned interiors of aircraft, improved protective clothing, better methods for overcoming the effects of the conditions imposed by environment, more effective means of controlling fires in aircraft, and stricter discipline, following careful instruction and study of the proper methods of conduct to prevent frostbite, injuries in crash landings, and parachute accidents

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AN EMERGENCY SURGICAL PLAN IN AN ARMY AIR FORCE HOSPITAL*

LT COL HARRY J WARTHEN, JR, M C, A U S

AMARILLO ARMY AIR FIELD

AMARILLO, TEXAS

ALL ARMY AIR FORCE HOSPITALS have organized, or are in the process of organizing, an emergency surgical plan by means of which catastrophes may be met and successfully dealt with

The advantages of a plan of this type are readily apparent. Plane crashes, though infrequent, occur without warning and often involve a considerable number of personnel. These accidents occur frequently at night when many of the surgical staff may be absent from the hospital. The injuries sustained by fliers are usually multiple and often of such severity that the rapidity with which medical aid is obtained determines the outcome to a greater degree than in the majority of accidents originating on the ground. In addition to accidents associated with flying, Air Fields are subject to the hazards inherent in all posts containing a large number of soldiers and motorized equipment. Military posts are also usually located near major railway and highway junctions and, thus, are not infrequently called upon to give emergency treatment to civilians as well as soldiers injured in nearby transportation accidents.

The plan adopted by one Army Air Force hospital to meet surgical emergencies will be outlined. While it is primarily designed to aid in treating injuries arising in military personnel, it would lend itself equally well to the needs of a civilian hospital in the handling of accident cases.

At the beginning, the plan consisted of a notice posted on the Surgical Bulletin Board entitled "Catastrophe Assignments," which reads as follows:

"Catastrophes, involving the injury of a number of persons, occur rarely. Because of the infrequency of such emergencies, considerable confusion may attend the handling of these conditions. In an effort to prevent this, the following outline is prepared:

1. If an emergency of such proportions arises during after duty hours, the Surgical Officer of the Day will be responsible for the notification of the Chief of Surgery, The Chief of Section or Sections involved, The Administrative Officer of the Day, The Anesthetists, Surgical Nurses and Operating Room Coopersmen.

2. The Surgical Officer of the Day will be in charge until the arrival of the Post Surgeon, Chief of Surgery, or Chief of a Surgical Section.

3. The number of Medical Officers summoned will be determined by the Post Surgeon or the Chief of Surgery, or their representative.

4. The telephone numbers of the members of the Surgical Service may be obtained below.

5. The Administrative Officer of the Day and other members of the

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Medical Administrative Corps designated by him will be responsible for maintaining order, checking clothing and valuables and safeguarding public property

6 The Hospital and/or Post Chaplain must be notified immediately in any major accident or whenever a death may result

7 In event the services of several Surgical teams are needed, the following tentative assignments are made

<i>Surgical Clinic Room</i> (Ambulatory Cases)	<i>Burn and Shock Room</i> Chief of Gen Surg,	<i>Operating Room No 1</i> (Major or minor Surgery)
Ward Officers on A-5 and A-9	Surg O D and Anesthetist	G U and E E N T Staff as needed
		Corresponding Ward Officers
<i>Operating Room No 2</i> (Major Surgery)		<i>Operating Room No 3</i> (Major Surgery)
Chief of General Surgery		Chief of Orthopedics and
Ward Officers on A-11 and A-15		Orthopedic Staff "

For the benefit of those who are not familiar with the term "Surgical Officer of the Day," it should be said that he represents the surgical service during off duty hours when other members of the staff may be absent from the hospital. He is responsible for the care of all surgical hospital patients as well as emergency treatment for those brought to the accident room. This assignment rotates among members of the service and the officer on duty corresponds to a resident in a civilian hospital.

The directions contained in this outline are all simple and self-evident and should occur to the Officer of the Day even if he chanced to be the most junior man on the staff as we should assume he will be in setting up any system. The difficulty lies in the fact that when confronted suddenly with a number of injured persons the surgeon is prone to go from one to another inspecting their wounds in an effort to decide which one needs his attention first and neglects to summon additional aid until valuable time has been lost. If he stops to telephone other members of the staff, he may feel that he is neglecting critically injured persons. On the other hand, if he delegates this notification to a nurse or corpsman, there is a strong possibility that someone will be omitted who should be called. This is especially true of the administrative Officer of the Day, who corresponds to the night superintendent of a civilian hospital and of the chaplain who should always be notified in any major accident.

A check list of this type would remind the surgeon, or any one he might delegate to handle it, of all persons who should be called. The operating room assignments would also serve as a tentative guide but could be altered readily depending upon circumstances.

After this plan had been in operation a short time the thought occurred that surgical catastrophes were not confined to mass injuries, but that a single emergency inadequately, or improperly treated, or a preventable death

occurring in the operating room, constituted a surgical catastrophe just as truly as a plane crash. The difference is a quantitative, rather than a qualitative one. In view of this, the plan was enlarged to include all of the more common emergency conditions that might arise on the wards, in the operating rooms, or on the post.

All equipment that might be needed in the treatment of emergencies was placed in one room in the surgical pavilion. This room was chosen due to its proximity to the operating rooms and the surgical wards. Each

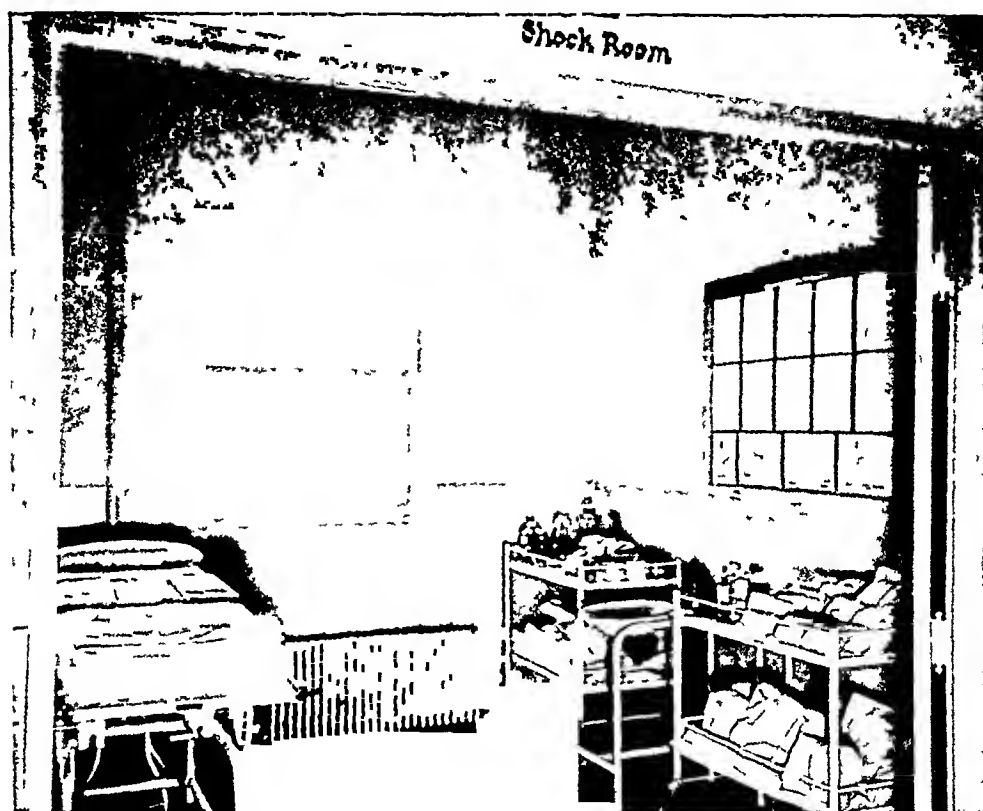


FIG 1—View of shock and emergency surgery room. This room is situated close to the operating room, the surgical wards, and the emergency room for the treatment of out patients.

surgical specialty was requested to prepare packs permitting immediate treatment of emergency conditions arising in that specialty.

Three surgical carts were stocked with medications, sterile instruments and dressings. One cart contained plasma, sterile water, vaselined gauze, machinist waste, sterile dressings, stockinette, wooden splints, mineral oil and other supplies needed in the treatment of burns. A second cart contained sterile packs permitting immediate tracheotomy, thoracotomy, craniotomy, and repair of vascular and nerve injuries. Intravenous and transfusion sets as well as sterile gowns, gloves and linen were included in this set-up. It was not anticipated that major procedures would be carried out in the emergency surgery room or by junior members of the staff, but it was felt desirable to have all equipment of this type in a central location familiar to every member of the surgical staff. A third cart was stocked with dressings and instruments needed in the repair of the more common injuries involving the soft parts.

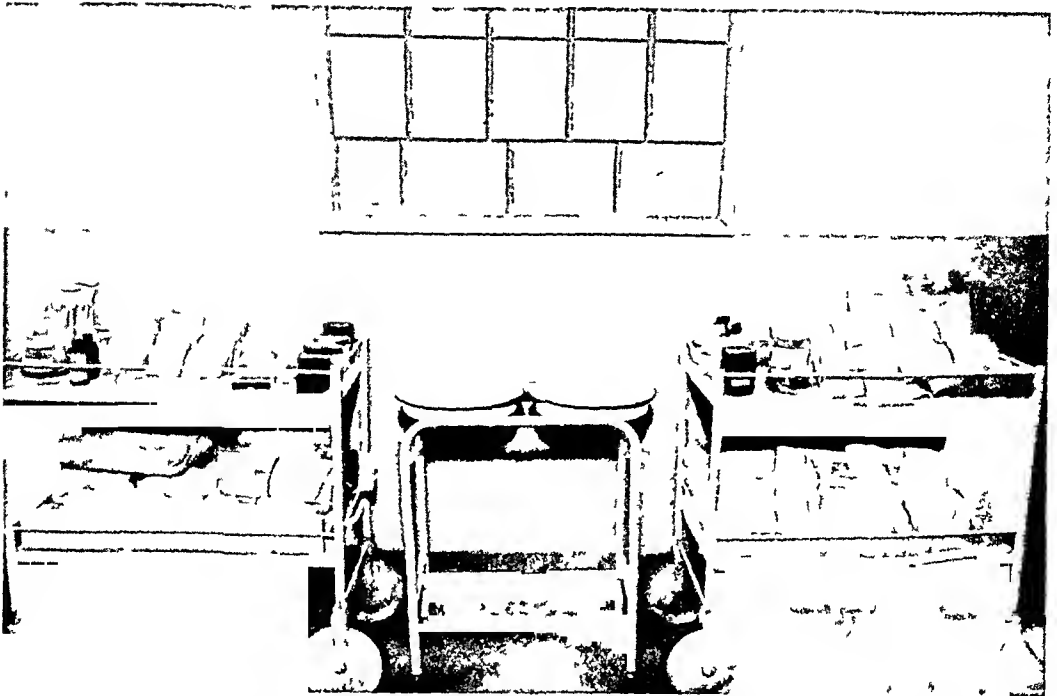


FIG 2—View showing one side of emergency room. The dressing cart on the left contains equipment to be used for the treatment of burns. The cart on the right contains sterile packs. The contents of each is clearly noted on outside labels. These packs will permit emergency procedures to be carried out with a minimum of delay. Thoracotomy sets, tracheotomy sets, arterial suture instruments and various other sterile equipment are included in container.

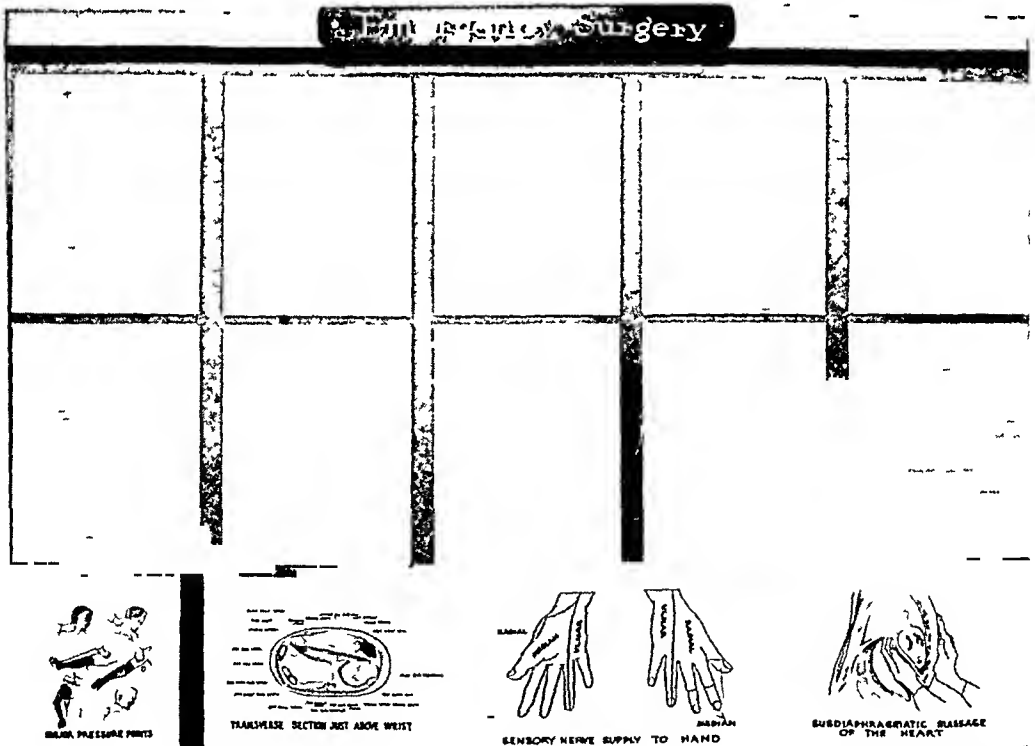


FIG 3—View showing Emergency Surgery Bulletin Board with outline of first aid treatment, tests recommended in certain conditions, and operative aids to guide surgeon in special procedures. For example of conditions listed on first sheet of this outline, (see text)

An important feature of these sets is the conspicuous labelling of all instruments and supplies contained in the packs. This conserves both time and sterility by preventing the opening and contaminating of packs containing unwanted material. Additional equipment of an emergency nature is contained in this room. A resuscitator and oxygen tanks are available in case of drowning or illuminating gas poisoning. A drug box is at hand which contains all of the more common emergency medications. Each ampoule is held in a designated space and when the box is opened the name, dose and indication for use of the medication appears on the under surface of the lid immediately above the drug described. Alcohol sponges with sterile syringes and needles are also contained in the drug box to prevent loss of time. Every effort has been made to leave as little to chance and memory as possible. Frequent inspections are made to insure that supplies are replenished promptly after use.

Probably the most important feature of the emergency room is a large bulletin board which contains in alphabetic order the recommended treatment for all anticipated surgical emergencies. Some of the procedures are not strictly emergency aids but rather reminders of tests which should be carried out before a patient is released, operated upon or admitted to the ward. While this system is designed primarily for the guidance of the younger men on the service it also contains data which may not be readily recalled by the older members of the staff when urgently needed. The antidotes for various poisons are listed and the insect and snake bites for which there are specific antivenoms are included.

This outline is not intended to encourage recent graduates to carry out procedures with which they are not familiar but rather to prevent them from overlooking commonplace measures which might be forgotten in the haste of the moment. Conspicuously displayed at the top of the bulletin board is a notice to the effect that the surgeon on call should be notified in all cases of severe injury or when a major operative procedure may become necessary.

This guide also serves another purpose. The technic of some of the more involved but infrequent surgical procedures are outlined, for example the method of handling cardiac tamponade by aspiration and the indications and operative approach for pericardiectomy. The recommended treatment for wounds involving major vessels and nerves and safeguards in handling injuries to the hand are included. Should the occasion arise, this would enable the surgeon operating to direct an assistant to leave the operating room, step across the hall and read in a moment the indications, technic and possible contraindications of a debatable procedure. It might be added that this aid has not been necessary since the plan was adopted, but the best guarantee against such a need arising lies in having the data readily available. The speaker can recall instances where he would have welcomed such a guide in handling unexpected surgical problems.

An example of the data contained on one sheet of this outline is as follows

"ALCOHOLISM 1. Symptomatic, draw blood for alcohol determination



FIG 4—Drug and dressing cabinet showing the labelling of each item in order that these materials may be obtained without delay when needed. Note the resuscitator and emergency drug box.

ANAPHYLACTIC SHOCK 1 Prophylaxis—intradermal test always before injection of serums (A T S and perfringens) and desensitize when indicated

2 Treatment—in addition to measures listed in traumatic shock, (See shock) give

A Epinephrine—0.5 to 1.0 cc of 1:1000 solution subcutaneously or 0.5 cc intravenously. Repeat in few minutes if necessary

B Atropine—0.001 ($\frac{1}{60}$ gr) subcutaneously has been recommended
APPENDICITIS, ACUTE 1 History, physical, rectal examination, complete blood count, urinalysis with microscopic Call surgeon on call
ASPHYXIA 1 Artificial respiration, resuscitator, oxygen (See cardiac arrest)

ASPIRATION OF PERICARDIUM 1 This should be done with a 17- or 18-gauge needle by costoxiphoid route (See Cardiac Tamponade, treatment of)

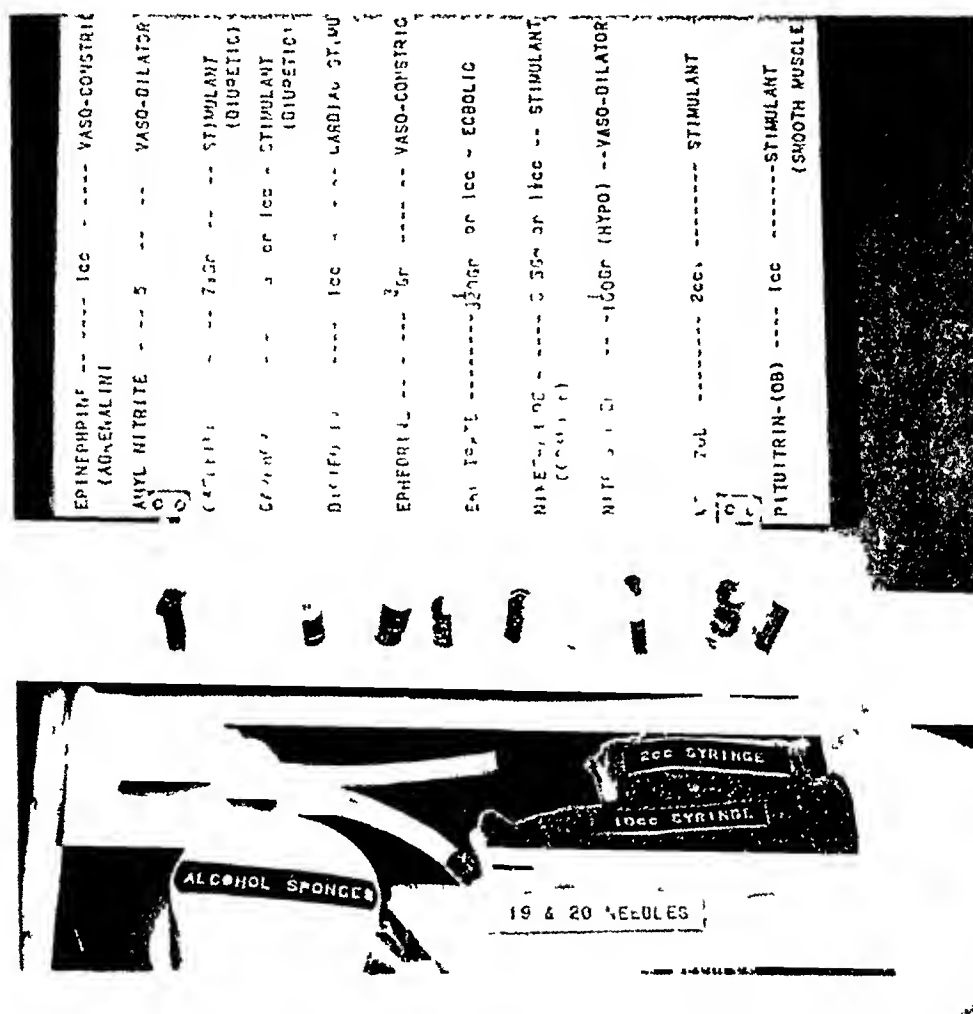


FIG 5—Drug box containing emergency drugs, needles, and sponges. The top of the box has the name, dose, and action of each drug, which is placed in an appropriate space beneath.

BERKOWS TABLE 1 (See Burns, general treatment of)

BLOOD VESSELS 1 (See Wounds of)

BITES 1 Black Widow spider Sedatives, calcium gluconate, normal saline I V, sodium pentothal I V if necessary

2 Dog Identify and observe dog If simple bite, treat as laceration If large—débride, tetanus toxoid if indicated (See tetanus)

3 Human. Débridement, sulfa generally, leave wound open

4 Scorpion Treat symptomatically

5 Snake Identify snake if possible Tourniquet, incise, suction, antivenom for rattlesnake, moccasin and copperhead Treat symptomatically

BLADDER 1. (See Wounds of)

Initial Treatment

BURNS 165 per cent of all deaths in burns are due to shock—*Avoid shock*

Local Treatment

Place patient on sterile sheet Surgeon must wear cap, mask, sterile gown and sterile gloves Everyone in burn room must wear masks

1 Débridement, consisting of opening large blisters and trimming loose skin

2 Remove gross contamination by sterile water, white soap and cotton pledgets, use abundance of water

3 Remove grease with sterile mineral oil followed by soap and water

Several sketches beneath the typewritten matter depict pressure points in the control of hemorrhage, the structures that pass through the wrist, the sensory nerve distribution to the hand, and a method of cardiac massage These drawings were included because occasions have arisen when this data would have been of value

In conclusion, it is desired that the following points be made clear

1 No claim for originality is made for the foregoing plan Many hospitals, no doubt, have devised various plans designed to meet surgical emergencies It is felt, however, that this system is a practical one and every effort has been made to make it as foolproof as possible

2 Although this plan was designed to meet the needs of a military hospital, it should lend itself equally well for use in civilian hospitals

3 The objection may be raised that the time and trouble necessary to organize and keep in readiness a plan of this type is not warranted by the occasional patient in which it might be of value This hardly is a valid criticism, for if such a system resulted in the saving of one life over a period of many years, its adoption would be justified

DISCUSSION—DR LOYAL DAVIS, Chicago, Ill There are two comments I would like to make upon Col Shands' very interesting paper One concerns high altitude frostbite, and the other injuries received by airmen from Oerlikon shells In our studies of high altitude frostbite it was found that the majority of cases were waist gunners who were subjected to the direct blast of cold air in temperatures often as low as -52 degrees, without the protection of plexiglass which gunners in other positions were afforded It is my understanding that this has now been remedied, with a very definite decrease in the number of casualties

Early in the history of the 8th Air Force in England, high altitude frostbite constituted one of the largest groups of casualties The oxygen bags became frozen because the masks were not of the demand type and because the tube leading into the bag was so small that saliva collected and froze This necessitated the removal of the mask and putting on the auxiliary mask Unfortunately, the method of fastening the mask onto the leather helmet consisted of fasteners which could not be grasped when flying gloves were worn, therefore, the airmen took off the gloves to fasten the mask in place Since the electrically heated suits and gloves were wired in series instead of parallel, the removal of even one glove threw the heat off for the entire suit At the altitude at which these men worked, it required only a few seconds for the most serious case of frostbite to occur

Attention was also called to many problems in the education of airmen, such as the fact that there is a relative anoxemia at an altitude of 10,000 feet, the proper care of

electrically heated clothing, wearing gloves which did not fit properly, and the tendency to trade clothing. All were factors in producing the high casualty rate for this condition. I am glad to learn, even though it was belated, and had not been anticipated, that steps have been taken to correct these technical and engineering difficulties. High altitude frostbite can be prevented and it is extremely important to prevent it, because once the lesion has occurred in severe form, there is either a loss of tissue or impairment of function which is permanent.

Many of the injuries from fragmenting Oerlikon shells are also preventable by the use of properly constructed protective flying clothing. A plastic helmet was proposed which would closely simulate the ordinary leather flying helmet and which would offer one-third more protection per unit weight than 1 mg manganese steel, and had very little weight. Other advantages of such a plastic helmet were pointed out and it was suggested that sheaths of similar plastic material could be inserted into the flying suits and provide protection for other parts of the body which would be adequate. The important advantage was, of course, that such protection did not weigh from 16 to 25 pounds, and would not constitute such a mental and physical handicap that the flyer would prefer not to wear the protection. This was presented for consideration to the Army Air Corps and the Quartermaster Corps, and it was also pointed out that it could be made applicable to the armored forces. I am glad to learn that the United States Navy and Marine Corps have adopted the principle of plastic protective clothing, and in field tests have proved its practicability. Perhaps, it still may not be too late to receive consideration for the use of army flyers and tank crews. This announcement has just been made in the Bureau News Letter of the United States Navy, November 24, 1944.

COL F S GILSPIE (B M C), Carlisle Barracks, Pa. I am glad to have the opportunity of telling you something of the work of your Medical Corps, which I was lucky enough to see in Normandy in July. I was greatly impressed by the speed of evacuation, and this was largely due to the efficiency of the forward medical personnel, the litter bearers and the drivers of jeeps which picked up their casualties right forward of Battalion Aid Posts. Wounded men were frequently picked up within a few minutes of being wounded. I do not think that nearly enough credit is given to these men for their gallant work. We are inclined to pat ourselves on the back for our wonderful hospitals, our wonderful surgery and our wonderful drugs, but none of these would have such good scope were it not for the splendid work of these corpsmen who get the patients rapidly back to where the other things are available.

Patients were speedily taken through the Battalion Aid Post, Collecting Company and Clearing Companies in the Divisional Area, in many cases on jeeps with improvised racks for litters and a Red Cross flag, these vehicles working in forward areas were respected by the Germans.

The most important life-saving surgery was being done by the platoons of Field Hospitals, working alongside Clearing Companies of the Divisional Medical Battalion, these units were reinforced by Surgical Teams and Shock Teams from the Auxiliary Surgical Group—and the combination was a most successful one. I saw some members of the same Auxiliary Surgical Group after the fighting in North Africa last year, and they were somewhat disgruntled because they felt they had not been given the opportunity of getting the forward surgery they had hoped for. They were rather looked on as "blackleg labor" trying to pinch the work from needy surgeons at Evacuation Hospitals and Clearing Companies. They were commanded by Colonel Blatt, and were affectionately (?) known as "Blatt's Bastards." They mentioned their grievance to me in Tunis and I said to them "Wait a bit, when casualties start occurring in large numbers they will be damned glad to get you"—and so it was.

Transfusion facilities with plasma were available at Battalion Aid Posts and Collecting Companies, and transfusion with whole blood was available at the Field Hospital Platoons. There, too, there had been a great improvement, in North Africa last year faith had chiefly been pinned to plasma but now there was a swing over to the use of whole blood, and surgeons were constantly demanding it for the severely wounded treated at Field Hospitals. When it was in short supply, there was a brisk reverse "lease-lend" process going on, with blood from British transfusion units, in fact a great many American soldiers were much improved by having good British blood in their veins. I know they received temporary benefit, let's hope it will be permanent.

The Surgical Teams were doing excellent work, and relays of them were working 24 hours a day. I do not think many lives were lost which could possibly have been saved. The statistics of results obtained are little short of amazing, but in this connection I should like to warn you against the tendency to use statistics like a drunkard uses a lamp post—more for support than illumination. I think you, over here, can rest assured that the rapid evacuation and early efficient surgical attention combined with adequate transfusion facilities with whole blood, now being made available from this country, are combining to give the wounded man a better chance of survival than has been possible previously.

DR J E J KING, New York, N Y. I should like to ask Colonel DeBakey whether he has any definite information on the intrathecal use of penicillin or sulfanilamide in early cases of perforating lesions of the skull where the ventricle is involved, and a second question on the use of these drugs with late cases of infection of the brain.

DR FRANK K BOLAND, Atlanta, Ga. As one of the facilities on the battle front which impressed him, Colonel Gillespie referred to transportation of the wounded to First Aid Stations and Evacuation Hospitals. It does not seem out of order, in this connection, to give credit to the man and agency which first inaugurated organized, adequate transportation, which has been developed to such a high degree of efficiency in the present war, especially by the Medical Department of our own Army.

During one of the wars in Central Europe, in 1863, Henri Dunant, a Swiss gentleman of means, was horrified by the neglect of wounded soldiers which he witnessed while visiting an area where a battle had been fought recently. Little attention seemed to be paid to the sufferers lying all around, and he called for volunteer stretcher bearers, and soon was carrying the wounded men to places where they could receive medical and surgical attention. This is said to be the first time such a systematic project was carried out. Thus, was born an organization destined to become the great Red Cross Society. So, as we praise the Red Cross for its marvelous contributions to the care and comfort of our fighting forces, let's not forget that it was this agency, through philanthropic Henri Dunant, that first taught armies modern transportation of the wounded, without which many triumphs of modern military surgery could not be utilized.

DR I A BIGGER, Richmond, Va. I would like to stress one or two points in connection with Colonel Warthen's paper. It is evident that military surgeons have somewhat belatedly recognized the importance of the early treatment of wounds by well-trained surgeons, but in some civilian hospitals the emergency care of patients who have been severely injured is still entrusted to relatively untrained members of the staff. Some of the reasons for this are legitimate, but I would like to emphasize the importance of having the hospital staff so organized that when seriously injured persons are admitted, senior as well as junior members of the staff are promptly notified. Colonel Warthen has described the manner in which this is accomplished in certain Air Force Hospitals. A similar plan could be used to advantage in civilian hospitals.

LT COL A R SHANDS, JR, Washington, D C (closing). I want to thank Dr Loyal Davis for his remarks on high altitude frostbite, no one in this country has had more experience with this condition than he has had. These injuries are preventable, as has been stated, and, certainly, the decrease in their incidence proves this point. It is principally a question of having improved flying suits and better protective equipment. Doctor Davis has asked about body and head armor, this certainly decreases the incidence of casualties. The missiles of low velocity definitely inflict less serious wounds than those of high velocity.

In conclusion, a word should be said about air evacuation. It is one of the great accomplishments in the transportation of the wounded in this war. More than half a million patients have been evacuated by air since the beginning of the war, and 55,000 from France alone since D-day.

LT COL MICHAEL E DEBAKEY, Washington, D C (closing). In reply to Doctor King's question, penicillin has been used intrathecally in the type of cases to which he referred, and the results are considered encouraging, although I am not in a position to give the actual figures.

AN ANALYSIS OF THE RESULTS OF THE SURGICAL TREATMENT OF 260 CONSECUTIVE CASES OF CHRONIC PEPTIC ULCER OF THE DUODENUM*

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BALTIMORE, MD

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IN 1939 I made a report upon the surgical treatment of 82 consecutive cases of peptic ulcer of the duodenum in the Johns Hopkins Hospital before the meeting of the American Surgical Association, at that time an operative technic was described which was based on certain anatomic and physiologic considerations that combined safety and efficacy, in a higher degree than the more conservative and also the more radical procedures. This operative procedure, however, like others carried out in the past, has limitations as a treatment for peptic ulcer of the duodenum, the determination of the type and extent of resection of the stomach and duodenum most acceptable from the standpoint of immediate and remote results will be ascertained only by comparison of reports of series of cases operated upon by different methods. The 260 patients herein reported have been operated upon by the same technic with the exceptions noted in which further resection became necessary because of postoperative complications. Thus the operative technic has been as nearly constant as possible.

Because of the fact that the series is composed of private patients, follow-up examinations could be carried out from time to time for a period of two to ten years by the physicians referring the patients for surgical treatment. Apparently a unique feature of this study has been the frequency of direct or indirect contact with the patients as well as their physicians. Every six months information has been obtained either personally or by letter from patients and often, as well, from their physicians. Thus, there have been no long periods of time during which a patient has been lost track of, nor a single instance in which a patient has failed to report. In this respect, postoperative studies are more easily carried out on private patients than on patients on the public wards. Because of this continuing follow-up, I came to know intimately a high percentage of the patients which enabled me to interpret more accurately the reports from both the patients and their examiners. In each case there had been commendable cooperation on the part of the patient in an attempt to obtain permanent relief of symptoms by faithful adherence to a medical regimen for periods ranging from 4 to 20 years previous to operation. Patients who for various reasons had not been conscientious in this respect were not included in the series. This series might, therefore, be classified as a specially selected group of patients who were subjected to surgical treatment because the complications of chronic peptic ulcer of the duodenum were not amenable to medical therapy.

* Read before the Fifty-sixth Annual Session of the Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

The rationale of the operative technic was as follows (1) The most active portion of the stomach from the standpoint of contractility, namely, the pylorus, the pyloric antrum and the fundus as far cephalward as the incisura angularis have been removed. By this procedure the acid-stimulating portion of the gastric mucosa lining the pyloric antrum was removed as well as one-third to one-half of the acid-secreting mucosa of the fundus. The removal of the mucosa of the pyloric antrum, therefore, takes away the major factors in the stimulation of gastric juice—acid and pepsin—by preventing the formation of the gastric hormone—gastrin. (2) Re-establishment of the continuity of the gastro-intestinal tract has been accomplished by the use of an antecolic gastrojejunostomy. The larger stoma created by this operative procedure brings about prompt emptying of the remaining pouch of stomach, thus, preventing the “pooling” of gastric juice and the retention of food products in the gastric pouch, which act as a constant source of stimulation for the secretion of digestive juice. (3) The Pólya-type of anastomosis permits free irrigation of the remaining pouch of stomach with the alkaline duodenal secretions, bile, and pancreatic ferments, and, therefore, produces a maximum degree of neutralization of the gastric contents. In this type of anastomosis following resection of the stomach, all of the duodenal contents *must* enter the portion of stomach remaining, which is not the case following other types of operations such as the Finsterei, Hofmeister, or Billroth II. (4) The flow of gastric contents is diverted from the ulcer-bearing portion of the duodenum into the jejunum. (5) A conservative resection followed by an antecolic gastrojejunostomy has a lower immediate mortality, and in the event of postoperative complications necessitating a further surgical procedure the technical difficulties of more radical resection are far less than those experienced when a retrocolic type of anastomosis has been employed with a primary resection (three-fourths to four-fifths) of the stomach. The necessity for performing radical resection routinely for peptic ulcer of the duodenum is not apparent when all but a relatively small percentage of these cases are satisfactorily treated by conservative resections with a lower immediate mortality.

Clinical Material—The number of patients forming the basis of this report totals 260, of whom (Table I) 83 per cent were males and 17 per cent females, a ratio of approximately 8 to 1. The distribution of these patients as to age was interesting, revealing the fact that 31 per cent were below and 69 per cent above 40 years of age. The majority of cases occurred in the fourth decade. Particularly in the male this period of life would probably represent the decade of greatest mental stress and strain due to business or professional worries or vocational hazards.

Symptoms—Each of the 260 patients in this series was referred for surgical treatment because of complications which developed as a result of the presence of a chronic peptic ulcer of the duodenum. Acute perforating ulcerations are not included in this report because it is felt that the surgical

problems presented by such cases differ from those of nonperforating duodenal ulcers. The complicating clinical features which were responsible for the discontinuance of medical treatment and the shift to surgery were mainly intractable pain, hemorrhage, and vomiting. In Table II an attempt has been made to group these patients according to the preponderance of the

TABLE I
AGE AND SEX RATIO IN 260 CASES
SEX RATIO

Sex	No. of Cases	Percentage
Male	216	83%
Female	44	17%
Total	260	100%

Age	No. of Cases	Percentage
Less than 20	2	1%
20 to 30	21	8%
30 to 40	57	22%
40 to 50	99	38%
50 to 60	55	21%
60 to 70	24	9%
Over 70	2	1%
Total	260	100%

different symptoms or signs. It is to be emphasized that the clinical course of a patient is often difficult to evaluate because not infrequently excruciating pain associated with penetrating ulcer of the anterior wall will so absorb the patient's attention that considerable amounts of blood in the stool will be overlooked or will be noticed only by a member of the family or the attending physician. Thus in Table II it is seen that 93 per cent of the patients had pain, but there was also bleeding and vomiting. In only 2 per cent was there vomiting alone, but in 49 per cent vomiting was associated

TABLE II
SYMPTOMS

93%, or 242 cases	Pain	
	Pain without bleeding	56% of 260 or 146 cases
	Pain with bleeding (below)	
42% or 109 cases	Hemorrhage	
	Bleeding with pain	37% of 260, or 96 cases
	Bleeding without pain	5% of 260 or 13 cases
49% or 127 cases	Vomiting	
	Vomiting alone	2% of 260, or 5 cases
		100% 260

with pain and bleeding. In only 5 per cent was bleeding present without a history of pain, and in each of these patients, the hemorrhages were very severe, yet 37 per cent of the 260, or 96 cases, not only suffered from bleeding but also had pain of a greater or lesser degree of severity. In the 42 per cent in whom bleeding occurred there was found at operation an ulcer in the posterior medial wall of the duodenum which had penetrated into the head of the pancreas, in every instance there was an associated chronic pancreatitis. The severity of the bleeding depended entirely on the

size of the pancreatic vessel which had been eroded—whether the pancreaticoduodenal artery itself or one of its larger branches. In every case in which one can obtain a history of bleeding the presence of a penetrating ulcer of the posterior wall of the duodenum can be confidently predicted.

One of the most striking pathologic observations in this series was the high percentage, 75 per cent, of the instances of multiple ulcerations of the duodenum. Scars of healed ulcers on the anterior and superior surfaces of the duodenum were often associated with ulcers of the posterior wall. In many instances the duodenum was actually a ligeneous tube. When one considers the fact that the symptoms and signs of which these patients complained over a period of many years were constantly changing from season to season, from pain to bleeding to vomiting, it is not to be wondered that ulcerations would have occurred in different regions of the duodenum. It appears conceivable that even though an ulcer of the anterior wall producing severe pain were to heal, the persisting disturbed physiologic mechanisms of the stomach should at a later date produce an ulcer of the posterior wall that would cause bleeding. The clinical history of the majority of the patients in this series suggests this sequence of events. Pain in the back probably due to involvement of the head of the pancreas was frequently associated with ulcers of the posterior wall. Specimens of the stomach in every instance showed infiltration of the submucosa with small lymphocytic cells, which has been interpreted as evidence of chronic gastritis. In some instances anamnesis reported a simultaneous occurrence of these complications, and again their appearance was sequential, so that division of these patients into definite groups under the heading of symptoms of pain or hemorrhage or vomiting would, with minor exceptions, be inaccurate and misleading. Practically all of the patients at one time or another, or at the same time, suffered from all the complications.

The chronicity and the recurring nature of these complications, with the necessary living restrictions which they imposed, had much to do with the decision of these patients to switch from a faithfully observed but unsuccessful medical regimen to surgery. Except in the few instances of exsanguinating hemorrhage, the inability to lead a normal life, due to constant pain, nausea, vomiting, indigestion, and the apprehension of repeated hemorrhages, rather than some catastrophic clinical incident such as perforation, almost fatal hemorrhage, or complete obstruction of the pylorus led the patient to seek such relief from surgery. In this respect private patients may well differ from those of the dispensary or the public ward. The former, becoming intolerant of relative incapacitation at an earlier stage, and having a more intelligent attitude towards surgical procedures, would be inclined to seek such relief before complications had assumed ominous proportions. Therefore, emergency operations for acute perforation or occasional massive hemorrhage should be considered separately from the elective surgery of the chronic duodenal ulcer. Undoubtedly, the problems

of both medical and surgical therapy presented by patients of different economic status vary to a large extent

Immediate Results—The immediate postoperative mortality in the 260 cases was 2 per cent, or five deaths. There have been no deaths in the last 160 cases. The cause of death of the five patients dying in the hospital was (1) shock following massive hemorrhage, which was observed too long before operation was performed, (2) sloughing of the duodenum, which had been mobilized too far down from the head of the pancreas for ulcer in the region of the ampulla of Vater, (3) transfusion reaction, (4) postoperative hemorrhage five weeks after the patient had been transferred to the medical service. The cause was unknown as autopsy was not performed. Since there was a loss of consciousness a cerebral hemorrhage may have ensued, and (5) bronchopneumonia. In only one death could the surgical technic be held responsible and that was the case in which the duodenum was dissected too far down from the head of the pancreas. This is the only instance in the entire series in which the duodenum has leaked. As a result of this experience, extensive mobilization of the duodenum has been abandoned, for regardless of whether the ulcer is excised or not, the attendant isolation due to closure of the duodenal stump will result in its healing *in situ*. In the exceptional case of massive hemorrhage with exsanguination, the duodenum has merely to be opened and the ulcer transfixed with a suture. The condition of the patient as a rule prohibits any more extensive surgical procedure, such as resection, at that time.

It would seem reasonable, therefore, to expect that in the future the immediate operative mortality in a similar group of patients might well be reduced even further. Even now, an operative mortality of 2 per cent provides a margin of safety as great as that of the most conservative operations for chronic peptic duodenal ulcer.

Remote Results—Until the cause of chronic peptic ulcer of the duodenum is known the surgical treatment of its complications must remain empirical. The primary objective of operative procedures in these cases is to protect the patient against complications such as hemorrhage, jejunal or marginal ulcer, pain and pyloric obstruction. The secondary objective is to prevent a recurrence of the same complications that followed the original duodenal ulcer. Regardless of the type of operation performed or the operator, where jejunal and gastric mucosa are brought together in the presence of acid chyme a certain percentage of patients will suffer from postoperative complications similar in all respects to the original complications of the primary ulcer for which operation was performed. In this follow-up study which has covered periods of 2 to 10 years in which either direct or indirect contact with the patient has been maintained every six months to a year, the classification of well, improved, and unimproved has been employed. Most postoperative complications manifested themselves in the first two years, but even to the tenth year patients have had to be shifted from the well to the improved column due to a late return of symptoms.

Table III presents an outline of the results as accurately as could be determined. It is to be noted that this study shows that of the 204 patients, or 78 per cent now considered well, only 172, or 85 per cent, have so far had no complications since operation. Thirty-two patients, or 15 per cent of the 204 known to be well, have had postoperative complications. It was necessary to operate again upon 22 of these, but they are at present well and completely free of signs or symptoms of peptic ulcer.

TABLE III
RESULTS ON 260 STOMACH OPERATIONS

Well	204 cases or 78%	Without complications	172 cases 85%
		With complications	32 cases 15%
		Reoperated 68% (22 cases) of above 32	
		<i>Complications</i>	
		Pain	12 cases 6% of 204
		Hemorrhage	12 cases 6% of 204
		Marginal or jejunal ulcer	12 cases 6% of 204
		Above with perforation	4 cases 2% of 204
		Adhesions	4 cases 2% of 204
		Average free acid (postoperatively) 13	
Improved	30 cases or 12%	Reoperated 16% or 4 cases of above 30	
		<i>Complications</i>	
		Pain	22 cases 77% of 30
		Hemorrhage	5 cases 17% of 30
		Marginal or jejunal ulcer	1 case 3% of 30
		Adhesions	2 cases 6% of 30
		Recurrent duodenal ulcer	1 case 3% of 30
		Average free acid (postoperatively) 36	
Unimproved	21 cases or 8%	Reoperated 15% or 3 cases of above 21	
		<i>Complications</i>	
		Pain	8 cases 38% of 21
		Hemorrhage	9 cases 46% of 21
		Marginal or jejunal ulcer	10 cases 54% of 21
		Recurrent duodenal ulcer	1 case 7% of 21
		Average free acid (postoperatively) 53	
Mortality	5 cases or 2%		
Total	260 cases 100%		

The average degree of free acid in this well group was low as compared to the improved and unimproved groups. Obtaining accurate figures for gastric analysis offered a difficult problem because of the different technics employed for obtaining this information. Some physicians preferred to base their estimate on the acid determination in the fasting stomach, others on the Ewald test meal, and still others on the alcohol and histamine method.

TABLE IV
ANACIDITY

40% (107 cases) of 260 had no free acid after operation
 8% (9 cases) of above 107 developed postoperative complications such as marginal ulcer or hemorrhage
 92% (98 cases) of above 107 remained well

It appears that the two first methods give a better insight into the normal function of the postoperative stomach than artificial stimulation by histamine. It is interesting to note that in 107 patients, or 41 per cent (Table IV), in

whom an acidity was reported following operation, 9, or 8 per cent, had complications, but the group with the lowest average acidity showed the highest percentage of well patients. In the group in which postoperative complications developed, although these patients were well and were so grouped, 10 patients recovered on a medical regimen. In 4 patients who had adhesions, obstruction of the efferent loop developed and necessitated a celiotomy to free the obstructed loop. The signs and symptoms of the complications overlap in the 32 cases (Table III). In only 2 instances was the ulcer actually a marginal ulcer, in all other instances the ulcers formed in the jejunum opposite the stoma or just distal to it in the efferent loop. In those that perforated, the perforation was on the anterior wall of the jejunum which had become adherent to the anterior abdominal wall. Penetrating jejunal ulcers that were associated with severe hemorrhage had eroded into the mesentery of the jejunum. In the case of patients listed as having jejunal ulcers verification was made at operation. Those cases in which the patients did not undergo a second operation were simply classified under pain, hemorrhage, or both.

Patients placed on the improved list ranged from those having very mild symptoms to those having more severe ones. The margin between well and improved was a narrow one, because if the patients had any symptoms or signs whatsoever they were not grouped with the well but with the improved. This group consists of 30 patients, or 12 per cent. In addition to the other data (Table III) it will be noted that the average postoperative free acid was 36 degrees. Also of interest is the presence of a recurrent duodenal ulcer in one patient following a previous pyloroplasty. The ulcer occurred at the junction of the gastric and duodenal mucosa anteriorly. In the improved group some were less improved than others and also demonstrated individual variation from time to time.

Under the classification of unimproved were placed the 21 patients, or 8 per cent, who have resisted completely both surgical and medical therapy. Further resection in three instances in which a very radical operation was performed also failed to protect the patients from a continuation of pain and hemorrhage. It is of interest to note that all of the patients in this group were of a sensitive, high-strung type in which there was a pronounced degree of psychobiologic lability. The average free acidity in this group following their primary operation was 53 degrees, which was much higher than was noted in the well or improved groups. In a consideration of the complications following conservative resection on the 260 patients of this series (Table V) it is noted that pain occurred in 42, or 16 per cent. This pain was assumed to be from a jejunal ulcer and in all instances was referred to the left upper quadrant of the abdomen. This was to be expected, for the pouch of the stomach remaining after resection is located in that region of the abdominal cavity when an antecolic gastrojejunostomy is employed. Marginal or jejunal ulcer occurred in 23 cases, or 9 per cent. In Table VI a summary of the data of this subject is given. A matter of interest which

is not shown in Table VI is that one patient was operated upon five times, four times for postoperative jejunal ulcer. This patient, a medical house officer, is now well after having practically all of his stomach removed. Two patients had three additional operations, and three patients required two later resections, but are now well. Table V also shows that the preoperative

TABLE V
POSTOPERATIVE COMPLICATIONS OF 260 CASES

Complication	No. of Cases	Percentage
Pain	42	16%
Hemorrhage	26	10%
Marginal or jejunal ulcer	23	9%

COMPLICATIONS IN RELATION TO PREOPERATIVE SYMPTOMS

Symptoms	Complications		
	Pain	Bleeding	Ulcer
Pain without bleeding	9% (22 cases)	3% (7 cases)	4% (10 cases)
Pain with bleeding and vomiting	8% (20 cases)	8% (19 cases)	5% (13 cases)
RESULTS ON 260			
With complications		32% or 83 cases	
Without complications		66% or 172 cases	
Mortality		2% or 5 cases	
		100% 260 cases	

signs and symptoms have very little relation to the probable postoperative complications. Altogether, taking into consideration the entire series, it is seen that in 83 patients, or 32 per cent, complications developed whereas 172, or 66 per cent, remained well. Five cases, or 2 per cent, died following the operation. The sources of bleeding determined were (a) from the mesenteric vessels of the jejunum, often severe, and (b) from multiple erosions

TABLE VI
MARGINAL ULCERS

9% (23 cases) of 260 developed jejunal or marginal ulcers
67% (15 cases) were reoperated out of above 23 cases
Present results of 15 cases reoperated
Well 80% (11 cases)
Improved 20% (2 cases)
Unimproved 20% (2 cases)
33% (8 cases) of above 23 cases were not reoperated
Present results all unimproved
Gastric acidity Preoperative for marginal ulcer—Average G A 36 free acid
Postoperative for marginal ulcer—Average G A 12 free acid
Symptoms of those with marginal ulcers
33% (8 cases) had hemorrhage
20% (5 cases) perforated
37% (10 cases) had pain alone
100% 23 cases—Total

of the jejunum, more often not serious. Table VII shows that 26, or 10 per cent, of the 260 patients suffered from postoperative hemorrhage of varying degrees of severity. Of these 38 per cent were again operated upon. One of them, who died from hemorrhage following operation elsewhere, had been classified as unimproved. Among those treated surgically and classified as improved were the patients having only occasional slight bleeding following operation which was detected by examination of their

stools Sixteen patients, or 62 per cent, were treated medically with the greater number falling in the improved and unimproved groups There were no fatalities among the 16 patients treated medically The source of bleeding in this group of patients, of course, was not determined, but none of these seemed to be more than temporarily incapacitated

TABLE VII
HEMORRHAGE

10% (26 cases) of 260 had postoperative hemorrhages	
38% (10 cases) of above 26 cases were reoperated	Present results
Well	50% (5 cases)
Improved	24% (3 cases)
Unimproved	16% (2 cases)
62% (16 cases) of above 26 cases were not reoperated	
	Present results
Well	44% (7 cases)
Improved	12% (2 cases)
Unimproved	44% (7 cases)

OPERATIVE TECHNIC

A midline incision has been employed because exposure of the lesser curvature of the stomach, and, thus, the left gastric artery and coronary vein, is more easily accomplished with less vigorous retraction by this route than through a high right rectus incision The less the degree of retraction the better the relaxation of the abdominal wall In the upper abdomen the midline incision traverses the linea alba which is the most avascular portion of the abdominal wall Obviously, there is no interference with the nerve supply to the rectus muscle or further weakening of that structure from direct trauma in splitting its fibers The round, or falciform ligament of the liver lies immediately beneath the linea alba, but under the right lip of the incision, the reflection of the peritoneum to cover the ligament may be incised and the entire body *i. e.*, ligament, fat and peritoneum, reflected laterally When the peritoneum is incised somewhat to the right of the reflection of the round ligament, it is not necessary to suture the edges of the former when closure of the abdomen is made The round ligament falls into its normal position covering the posterior surface of the wound as a peritoneal flap, when the linea alba and thus the abdominal wall is closed

The location of the common duct and its point of disappearance behind the upper part of the second portion of the duodenum has been made a routine preliminary step in the operation The knowledge of the position of this duct affords not only more confidence but also more safety in a liberal mobilization of the second part of the duodenum for resection of ulcers in this region At the same time, such a free dissection enables the operator to effect a more secure closure of the duodenal stump The left gastric vessels and right vagus nerve are then divided and ligated with medium "c" silk Following this, vessels running in the gastrohepatic and gastrocolic as well as the duodenohepatic and duodenocolic ligaments are individually clamped and ligated with "c" silk Thus, the entire lower fifth or pyloric antrum of the stomach, together with the first and upper two-thirds of the second portion of the duodenum are thoroughly mobilized and

the latter freed from the head of the pancreas. A medium-sized Payr crushing clamp is now placed across the body of the stomach at approximately the midportion of the stomach. The stomach is divided and the posteromedial surface of the duodenum is freed from the head of the pancreas. Due to the fact that the common duct lies between the head of the pancreas and the medial wall of the duodenum, a portion of the latter may be removed

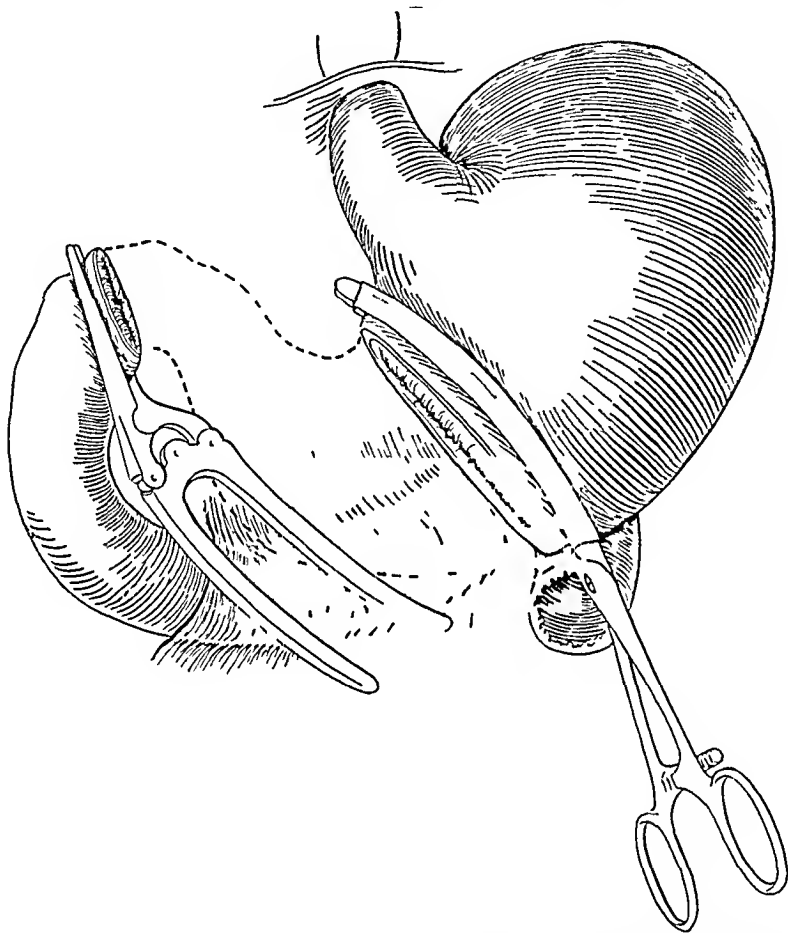


FIG 1—Dotted line demonstrates portion of stomach removed which includes first part of duodenum, pylorus, pyloric antrum and fundus up to incisura angularis

without danger of injury to the former. The duodenum, having been mobilized may be clamped across with a small Payr crushing clamp, or, and in some instances a method to be preferred is to open the duodenum and after inserting the finger into the open end to dissect the ulcer on the finger very much like the technic employed in mobilizing a hernial sac. The pyloric antrum, and pyloric sphincter, together with a portion of the fundus of the stomach are then removed (Fig 1). The stump of the duodenum is closed with two layers of sutures (Fig 2) the first a continuous suture of "o" chromic catgut. This is placed underneath the crushing clamp in such a manner that the crushed tissue beyond it can be cut off without danger of cutting the suture line. The advantage of removing this crushed tissue, which will become necrotic, is obvious. With this type of suture only

viable tissue is turned in. Interrupted Halsted sutures of fine "a" silk are then used to invert the first continuous suture line. It is frequently a most gratifying surgical procedure if one inverts the duodenum from the midline laterally instead of in the vertical plane (Fig 3). The reason for this is that less of the duodenum need be freed from the head of the pancreas, which in some instances, because of penetrating posterior wall ulcers, may be a formidable undertaking and one fraught with danger due to the difficulty

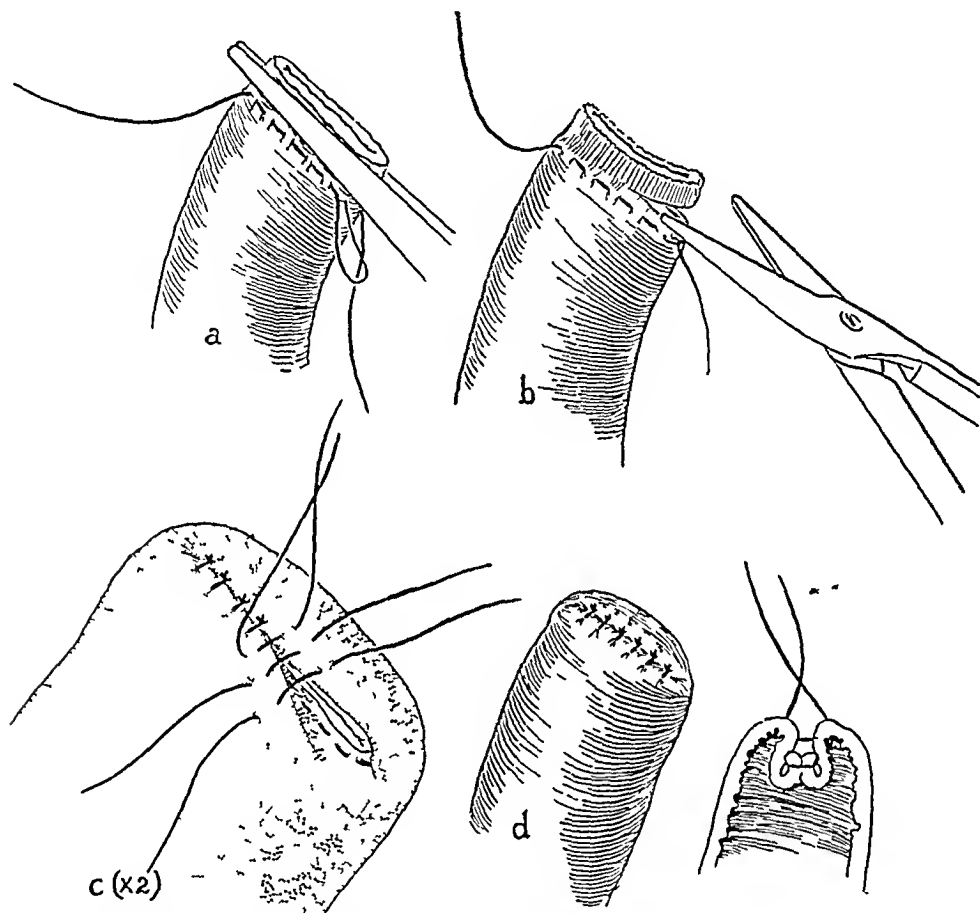


FIG 2—Method of closure of duodenal stump (a) Application of continuous mattress suture of O chromic catgut beneath crushing clamp, (b) trimming off crushing tissue distal to suture line, (c) Turning in duodenal stump with interrupted Halsted sutures of fine silk, (d) Turn in completed, showing cross section of inturned portion of duodenum

of turning in the scarred base. All bleeding points about the head of the pancreas are transfixed with fine silk. Care is taken to insert a small part of the beginning or extreme right portion of the gastocolic omentum between the raw surface of the head of the pancreas and the duodenum, in order to prevent any possibility of digestion or erosion of the stump of the latter. Attention is then turned to the reestablishment of the continuity of the gastrointestinal tract. Due to the relatively small segment of stomach removed, a short-looped antecolic gastrojejunostomy can be performed readily and without the necessity of an entero-enterostomy. The colon and greater omentum are returned to the peritoneal cavity by shunting them to the left of the proximal loop of the jejunum. When this latter portion of the intestine is sewn to the cut-end of the stomach, the distance between

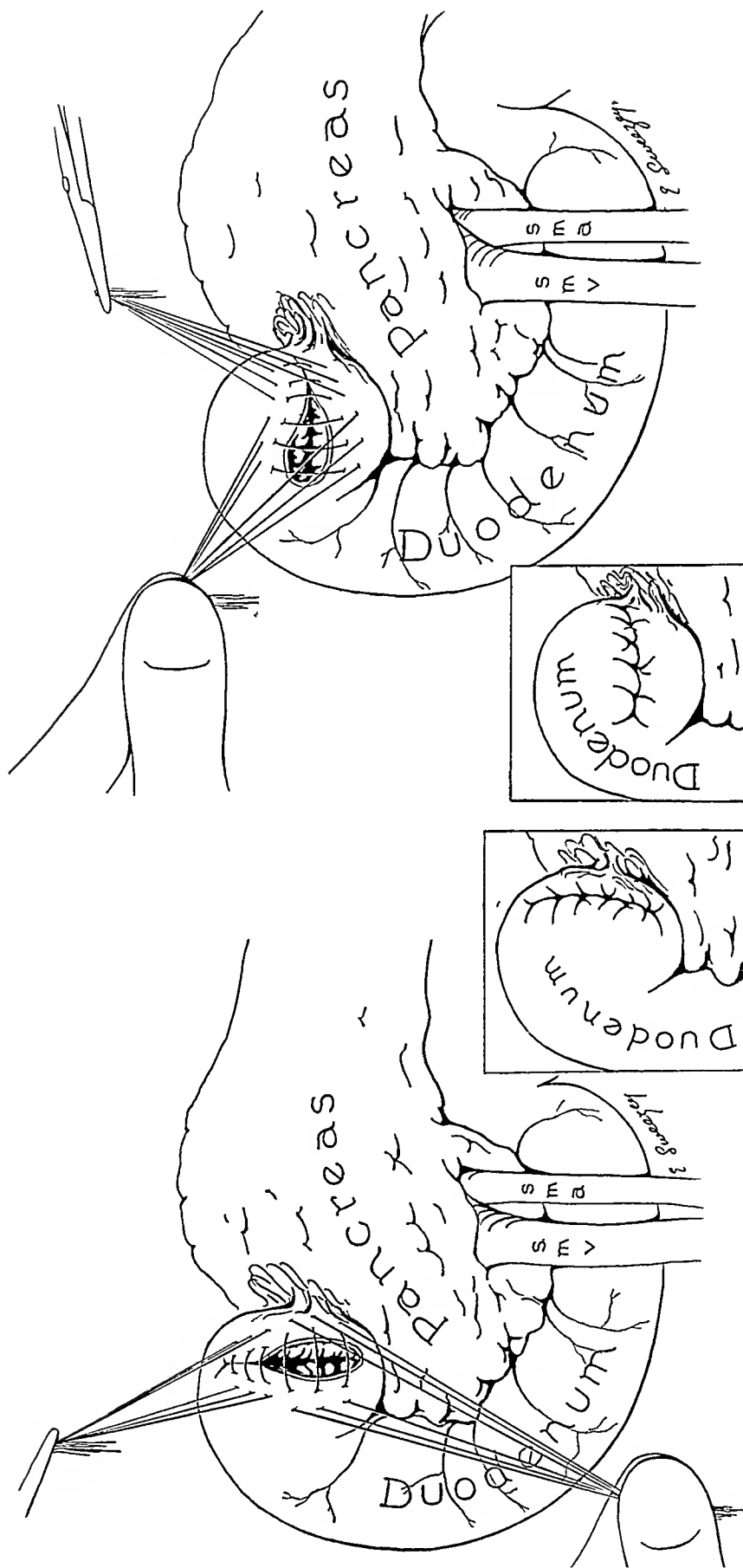


Fig 3 —Demonstrates the vertical and lateral closure of the duodenal stump

Tréitz's ligament and the beginning of the gastrojejunal anastomosis at the lesser curvature of the stomach is only three fingers' breadth. A few centimeters proximal to the Payr crushing clamp, a noncrushing clamp is placed

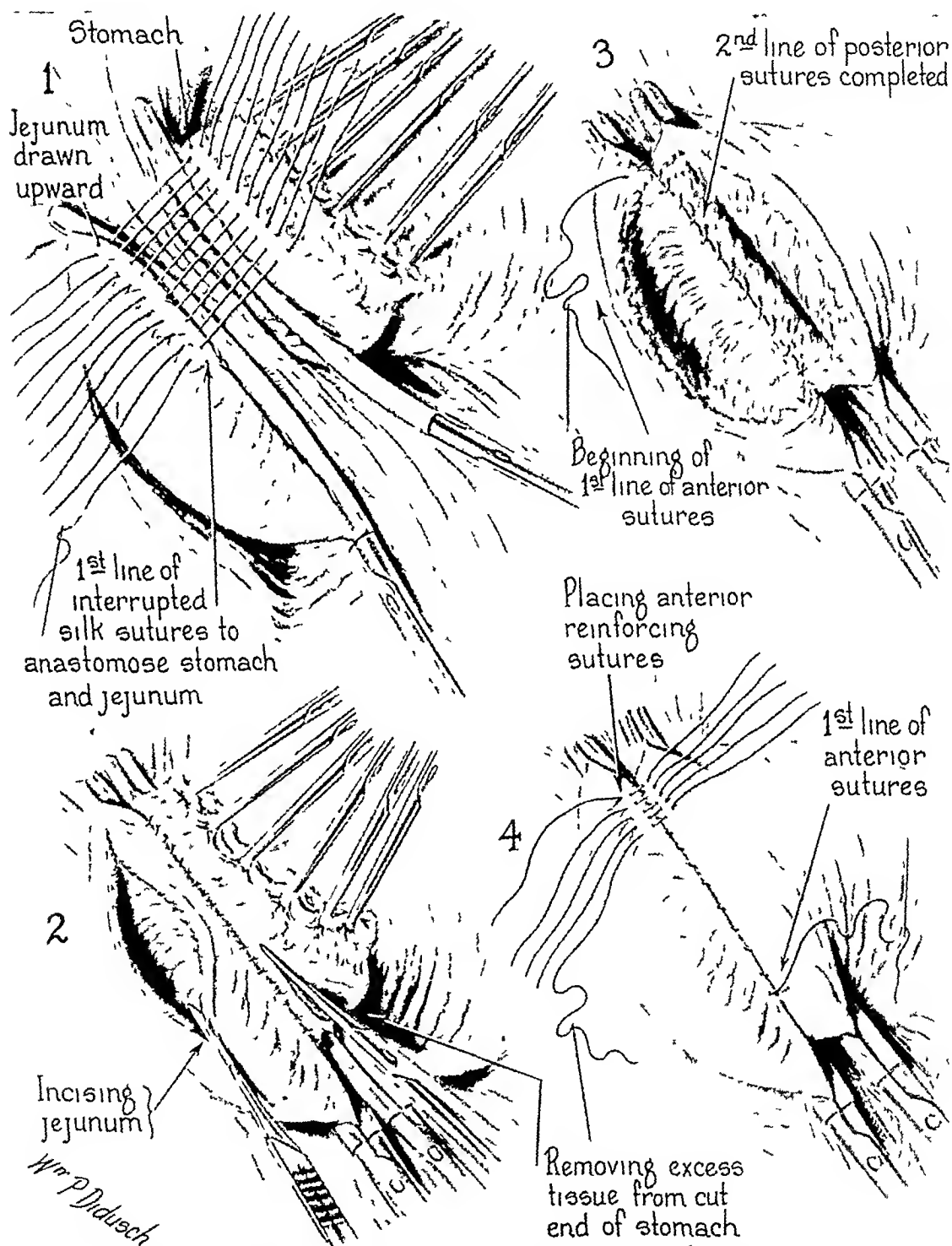


FIG 4—Method of reestablishment of continuity of gastrointestinal tract by antecolic gastrojejunostomy. Crushed tissue is removed from the stump of the resected stomach.

upon the stomach and a similar one upon the jejunum. Gauze webbing is used to cover the blades of the noncrushing intestinal clamps in preference to rubber, the former having the advantage of being far less bulky and

affording much greater purchase, and, therefore, capacity to hold with less pressure exerted on the tissue through the blades of the clamp. The Payr crushing clamp is then removed and mucosa clips are placed upon the cut-end of the stomach embracing only the crushed portion of the stomach wall, while the imprint of the Payr clamp is plainly visible (Fig 3). Halsted interrupted fine silk sutures are then inserted about 0.5 centimeters apart as the posterior suture line. The entire line is placed before any of the sutures are tied, thus, allowing more room for inserting successive sutures accurately than if they are tied as placed. The crushed portion of the stomach wall, which has been grasped by the mucosa clips, is then excised. The posterior interrupted suture line is much more easily and accurately placed if the mucosa clips are allowed to remain on through this step in the operation. This is due to the fact that the clips, lying in such a manner that their handles point to the left, cause the posterior wall of the stomach to be thrown anteriorly and place it in a more convenient position for suturing. The jejunum is then opened and a continuous suture of No. 1 chromic catgut is placed as an internal suture line in both the posterior and anterior lips of the mucosa. These stitches are locked only at the ends, to prevent any chance of diminution of the stoma by constriction. The final anterior row of Halstead interrupted "a" silk sutures is placed in position before the noncrushing intestinal clamps are removed, but they are not tied. This is accomplished after the stomach and intestine have been released from the noncrushing clamps. In this manner the sutures are more accurately placed and then tied without exerting any tension on the wall of the viscera. A couple of interrupted sutures are placed between the lateral wall of the proximal loop of the jejunum and the transverse mesocolon to prevent a loop of jejunum lower down from slipping through this potential opening. The anastomoses have so far been made isoperistaltic with the proximal loop sewn to the lesser curvature (Fig 4).

The abdomen is closed in the following manner. The linea alba with interrupted double medium silk and the skin with interrupted fine silk sutures.

DISCUSSION—In what may be termed a continuing study of 260 patients who were operated upon for peptic ulcer of the duodenum of from 4 to 20 years' duration, the results indicate that only 204 patients, or 78 per cent, should be regarded as well, 30 patients, or 12 per cent, as improved, and 21, or 8 per cent, as unimproved. The immediate mortality was 2 per cent, with no deaths occurring in the last 160 cases. These patients were operated upon because of complications arising from a chronic peptic duodenal ulcer that would not respond to medical treatment. The complications consisted of intractable pain, hemorrhage, and vomiting associated with pyloric obstruction. In other words, the duodenal ulcer, or ulcers, had continued to erode, eventually involving contiguous structures such as the pancreas, in spite of the fact that those patients had cooperated to the fullest extent in following a strict medical regimen. Because these patients, generally speaking, had a more intelligent and better informed attitude than ward patients, they

had sought operation before their complications had so reduced their vitality as to make any operation precarious

A conservative resection of the stomach and first portion of the duodenum was performed because resection, while far from ideal, was thought

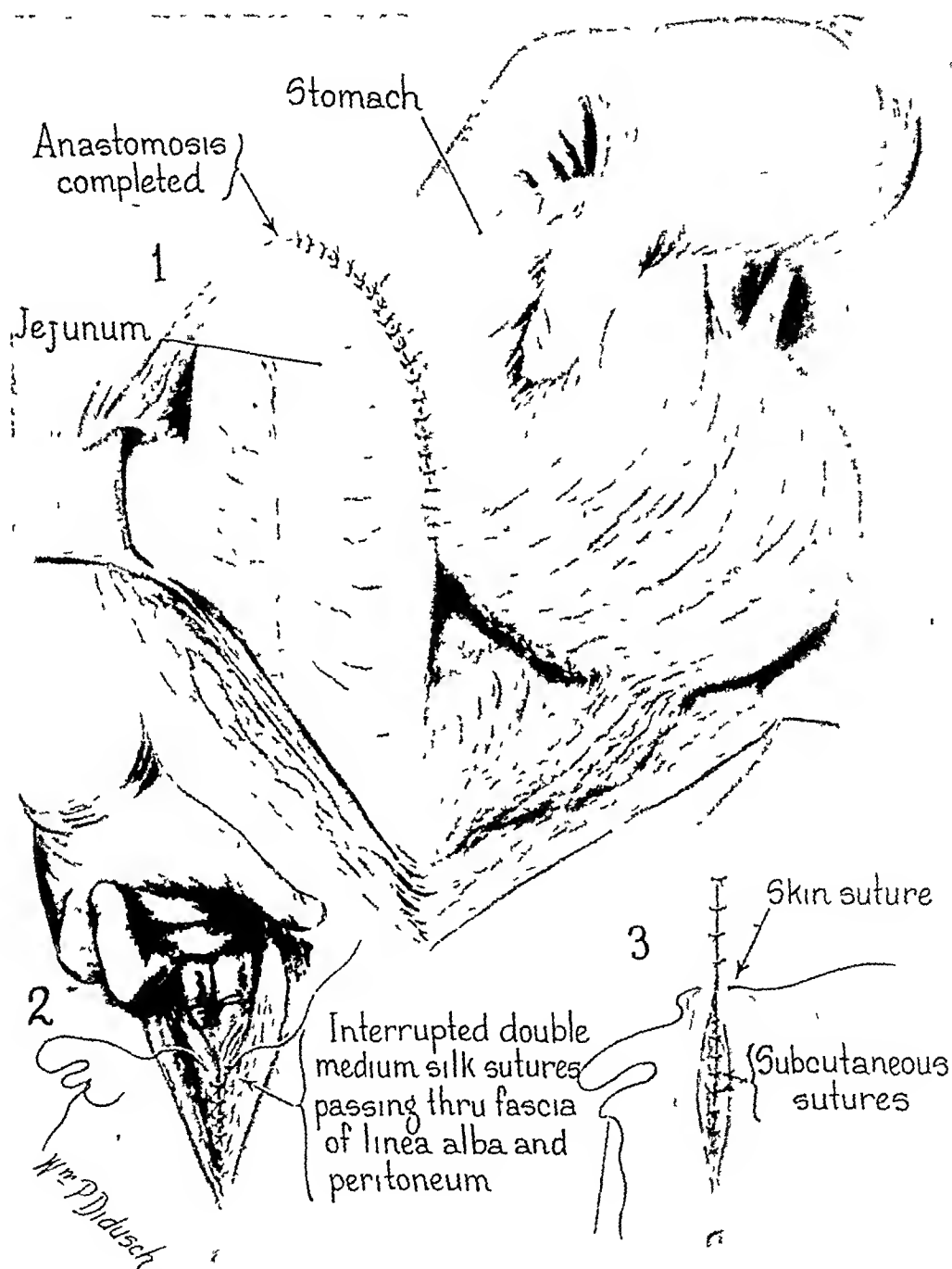


FIG 5—The anastomosis completed, antecolic gastrojejunostomy—Polya Balfour type

more efficacious than less radical procedures such as gastro-enterostomy. The advantages in the type of operation employed will be discussed later. In brief review, the surgical procedure has been (1) to remove the pylorus, pyloric antrum, and a portion of the acid-secreting mucosa of the fundus; (2) to shunt the flow of acid chyme and food away from the ulcer-bearing

area of the duodenum, and (3) to employ a type of anastomosis which insures the maximum irrigation of the remaining pouch of stomach and at the same time prevents pooling of gastric juice and food due to delayed emptying. The rationale of the operative procedure, an antecolic gastrojejunostomy, is based upon the following considerations: (1) If the flow of gastric contents can be diverted from the duodenum chronic peptic ulcers of this structure will heal or will fail to recur when excised. In over 75 per cent of the patients in this series the ulcers were left *in situ* and apparently healed. (2) The operation must protect the patient from the development of post-operative complications in the jejunum such as peptic jejunal ulcers or hemorrhagic jejunitis. (3) The original operation must have been so performed that in the event of jejunal complications secondary operations may be carried out with minimal technical difficulty and operative mortality.

All observers apparently agree upon the fact that chronic ulcer of the duodenum, with very few exceptions, will heal if put to rest by diverting the flow of gastric contents away from the ulcer-bearing area of the duodenum. Extensive and hazardous dissections of ulcers located in the lower portion of the duodenum are unnecessary. If the ulcer is on the posterior wall and has produced massive hemorrhage and the patient is in shock, the better procedure is simple transfexion or cauterization, or both, of the bleeding vessel in the base of the ulcer.

There seems to be a lack of unanimity of opinion, however, in regard to the extent of resection and the type of operation to be employed. Although it is difficult to estimate accurately the amount of stomach removed at operation, one usually thinks more of the organ has been resected than actually was removed because the size of the stomach varies. It is possible because of anatomic landmarks to arrive at a certain degree of uniformity in operative procedure. In this series, division across the fundus of the stomach, was made at right angles to the curvatures, greater and lesser, at the level where the left gastric vessels leave the lesser curvature and spread over the anterior and posterior surfaces of the stomach. This area corresponds anatomically with the incisura angularis. This procedure insures removal of roughly 50 per cent of the organ including the pylorus, the pyloric antrum, and about one-third of the acid-secreting area. The removal of the antral mucosa is felt to be important because of the elimination of the hormone gastrin, the chemical stimulant for the formation of gastric juice. Also removed is an indefinite amount of acid-secreting mucosa.

The results in this series seem to indicate that conservative resection of the stomach may be carried out with an immediate mortality as low as that following gastro-enterostomy. Therefore, this type of resection is to be preferred to gastro-enterostomy in the kind of case under discussion. The remote results also indicate that resection, regardless of the extent short of almost total gastrectomy, will not insure against the development of jejunal complications. This was demonstrated in this series in a few persons with pronounced ulcer diathesis and others upon whom it was necessary to operate

two, three four and even five times for recurring peptic jejunal ulcer. One point seems certain however, and that is that the majority of patients who are well are those with the lowest degree of free acid. There are a few who, despite high postoperative free acid, are asymptomatic, but they are exceptions to the general rule. The patients in the improved and unimproved groups tend to support this observation. Another well known and supporting fact is that peptic ulceration of the jejunum does not occur following gastric resection for carcinoma of the stomach. The success or failure of a resection of the stomach for peptic ulcers of the duodenum depends, therefore, in the majority of patients, on permanent reduction in gastric acidity under the normal circumstances of the patient's everyday life. This reduction is accomplished in three ways: (1) By removal of the acid-stimulating hormone gastrin, (2) by reduction of the acid-bearing area by partial removal, and (3) by neutralization of the acid juice by a thorough mixing with the alkaline jejunal contents. Individuals differ in the secretion of acid-pepsin gastric juices as they do in every other function of the human body but these results suggest that, either by neutralization of the acid gastric juice or by partial excision of the acid-bearing mucosa, the majority of patients in this series struck a favorable acid balance following this type of conservative resection of the stomach. Adequate mixing of gastric and jejunal contents and prompt emptying time of the remaining gastric pouch to prevent pooling of food and gastric juices are considered to be of great importance. The very low immediate mortality rate adds to the desirability of conservative resection. In the relatively small percentage of patients in whom evidence of persistence of high free acid is found together with either the signs or symptoms of jejunal erosion or ulcer, a further radical resection may be performed.

SUMMARY

The fact that patients in whom chronic peptic ulcer develops have a psychobiologic lability above normal is well recognized. The reason for the unstable clinical status observed in this postoperative study is, therefore, not far to seek. There are many shades and nuances between the well group and the improved group, and also among the individuals comprising these groups. Most of the postoperative complications appear to occur within the first two years, but they may occur at any time later. Gastric resection is the best method available at present for the treatment of the complications of chronic peptic ulcer of the duodenum but is not ideal in that it is only relatively better than less extensive surgical procedures. This report is made in order to serve as a basis for future comparison and study, and it may be said to result from a search for a surgical procedure which combines in the highest degree both safety and efficacy.

TRANSTHORACIC GASTRECTOMY FOR UNUSUAL LESIONS OF THE STOMACH*

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MALIGNANT TUMORS of the proximal portion of the stomach are relatively silent unless they cause obstruction of the cardia. Even after the symptoms of dyspepsia appear, diagnosis may be delayed because of difficulty in visualizing early lesions of the fundus by barium study. Extragastric extension into the liver, diaphragm, spleen or lesser peritoneal cavity, as well as the regional lymph nodes, is often present before the patient comes to surgery. Tumors of the cardia may extend some distance up the esophagus and tumors of the lower esophagus may invade the proximal stomach. Until recent years, these factors rendered most malignant tumors of the cardia and fundus inoperable. Even since the development of transabdominal total gastrectomy with esophagojejunostomy, the technical difficulties of working up under the dome of the diaphragm are considerable when there is extragastric extension of the tumor, and involvement of the diaphragm or lower esophagus may make transabdominal resection impossible. Within recent years, reports of transthoracic approach to these tumors have been increasingly frequent ^{1, 2, 3, 4, 5, 6, 7}

The advantages of the transthoracic approach are (1) more direct accessibility and better exposure of the involved structures within the abdomen, and (2) the ability to deal with extensions of the tumor in the diaphragm and lower esophagus. The disadvantages are (1) the possibility of infection in the mediastinum and pleura, and (2) somewhat longer operating time. To this may be added the reluctance of many abdominal surgeons to invade the thorax. Careful technic, avoidance of contamination, and meticulous attention to the details of anastomosis will minimize the danger of infection. The use of fine interrupted sutures of nonabsorbable material throughout is of particular value. Prophylactic use of the sulfonamides or penicillin may be of some importance.⁸ Gentleness, good hemostasis, and adequate replacement of blood loss, combined with expert anesthesia, make the operating time of little importance.

Preoperative Preparation—This need be no different than for any major gastric operation. Defective dental hygiene should be corrected. Hemoglobin, protein, and other chemical deficiencies should be restored to normal. Since few of these patients have gastric stasis, gastric drainage or lavage is not so important as in lesions of the distal stomach, but lavage of the esophagus should be done if there is obstruction at the cardia. The administration of dilute hydrochloric acid is advisable if achlorhydria is

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present, in order to reduce the bacterial flora. Establishment of an adequate blood level of sulfadiazine or the administration of penicillin in doses of 15,000 units every three hours for 48 hours preoperatively, may decrease the danger of infection.

Anesthesia—The most important factor in anesthesia is the expert anesthetist. He must have a full understanding of modern anesthesia and of respiratory physiology and must possess the ability to anticipate and prevent changes in the patient's condition. My preference has been for endotracheal ether-oxygen anesthesia, with thorough aspiration of the pulmonary tree at the end of operation.

Operative Technique—The patient is supported on his right side so that a field from the midline posteriorly to the midline anteriorly on the left side is available. An incision is made over the 8th, 9th or 10th rib according to the obliquity of the ribs, and the rib resected from the angle to the costal margin. This position and incision allows extension across the costal margin and upper left abdomen if this should be necessary. The thorax is explored and mediastinal lymph nodes palpated for evidence of metastasis. The lung is then packed away into the upper chest and the phrenic nerve crushed low at the side of the pericardium to immobilize the diaphragm and prevent tension on the suture lines postoperatively. The mediastinal pleura over the esophagus is incised as far upward as may be necessary and the incision carried across the diaphragm from the esophageal hiatus to the costal margin. Bringing the anterior end of the diaphragmatic incision to the same point as the anterior end of the thoracic incision allows the abdominal and thoracic cavities to be converted into one, if it is necessary to extend the incision onto the abdominal wall. The abdomen is explored for metastases and the operability determined. We have routinely removed the spleen in order to increase exposure and facilitate the rest of the procedure. The lower esophagus is freed from the mediastinal structures and the vagus nerves divided above the diaphragm. Section of these nerves considerably increases the mobility of the cardia. The greater curvature of the stomach is freed and dissection carried behind the stomach to the gastric vessels which are ligated and divided close to the celiac axis. This dissection is carried out retroperitoneally if there is involvement of the posterior wall of the stomach, removing the posterior peritoneum of the lesser sac down to the pancreas. The lesser curvature is freed along with the entire gastrohepatic omentum and the lymph nodes of the lesser curvature. The stomach and lower esophagus are now quite mobile and may be lifted almost to the surface of the thorax. The stomach is divided between clamps with the cautery as low down as necessary to get well below the tumor. It is possible with this exposure to perform a total gastrectomy, utilizing the jejunum for the subsequent anastomosis. Usually, however, a considerable portion of stomach may be left. Closure of the stomach is carried out with two layers of interrupted fine silk inverting sutures, and the tip of the greater curvature is sutured to the posterior thoracic wall to reduce tension on the subsequent suture line, as

advocated by Carter¹ The esophagus is divided between clamps and the specimen removed The proximal esophagus is emptied by aspiration through a tube which has been previously inserted from above, and aspiration is continued throughout the remainder of the anastomosis The esophagus is sutured to the anterior surface of the stomach for a distance of an inch or more to minimize tension An opening is made in the anterior surface of the stomach equal in length to the diameter of the esophagus and an



FIG 1—Case 1 Barium study showing deformity of fundus

open anastomosis carried out in two layers with interrupted fine silk sutures The anastomosis may be reinforced with any available tags of omentum Any fluid or clots remaining in the abdomen are removed by suction and about 25 grams of sulfanilamide crystals dusted about the anastomosis Margins of the diaphragm are then sutured to the stomach well down from the anastomosis so that there will be no pull on the suture line The remainder of the diaphragm is overlapped a distance of about one centimeter and closed with mattress sutures of interrupted silk The thoracic cavity is cleaned and dried and about 25 grams of sulfanilamide dusted over the surface of the diaphragm The chest wall is closed in layers with silk without drainage after the lung has been inflated by the anesthetist

Postoperative Care—One or two transfusions have usually been given during the operation These are supplemented by additional transfusions postoperative as indicated The esophageal tube which has been pushed into the stomach is connected with constant suction, which is maintained for about 72 hours, at the end of which time liquids may be cautiously given by

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mouth. Meanwhile, the usual postoperative supportive measures and the maintenance of adequate fluid intake parenterally have been carried out. Any accumulation of fluid or residual air in the left pleura is removed by aspiration at proper intervals. When fluids are started they are administered in amounts of one ounce every 30 minutes if tolerated well. This can rapidly

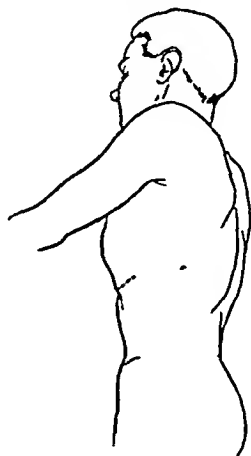


FIG. 2—Line of incision from angle of rib to costal margin. Incision is made over eighth, ninth or tenth rib according to obliquity of ribs.

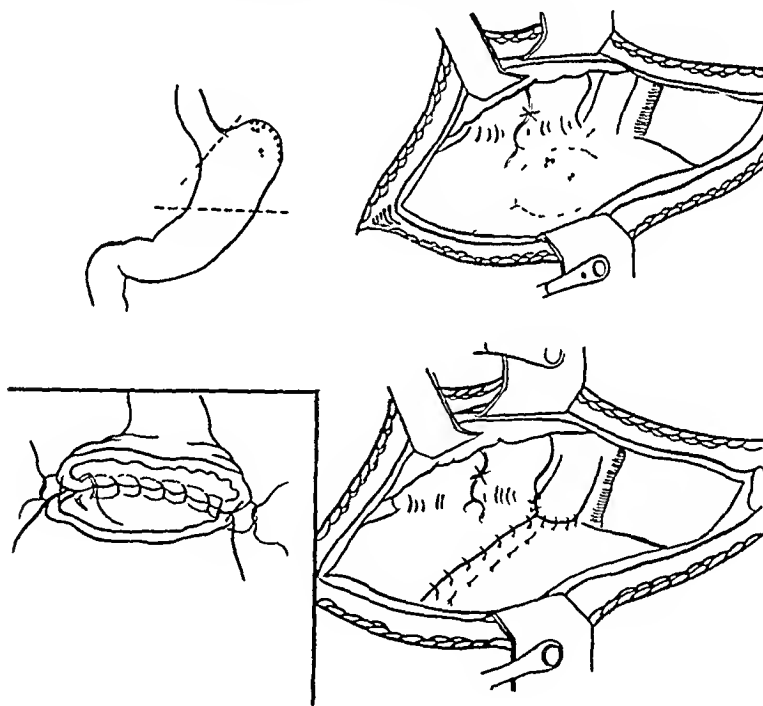


FIG. 3—Case 1—Upper left: Diagram of tumor and lines of resection. Upper right: Invasion of diaphragm by tumor with line of incision in diaphragm. "X" shows point of crush of left phrenic nerve. Lower left: End to end anastomosis of cardia and antrum. Lower right: Suture of diaphragm and closure about esophagus.

be stepped-up and the amount and consistency of feedings increased until at the end of ten days the patient should be on a full soft diet, and at the end of the third week should be taking a full normal diet.

Case 1—Register No. 213573. White, male, age 49.

Family and past histories were irrelevant. Present illness began about November, 1943, with dysphagia, regurgitation of solid food immediately after eating, and epi-



FIG 1—Case 1. Postoperative roentgenogram showing small normal appearing stomach

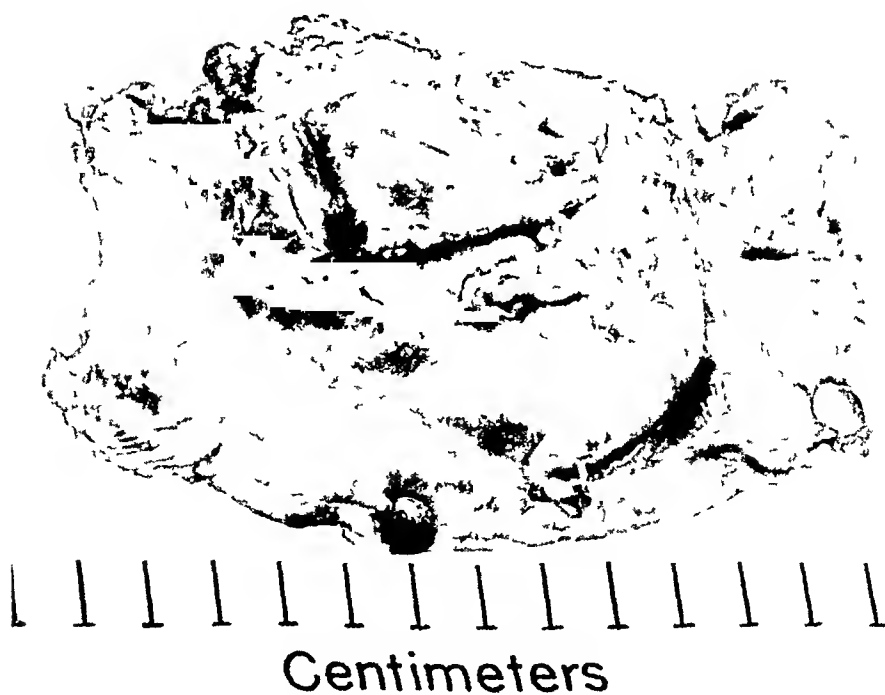


FIG 5—Case 1. Outer surface showing triangular portion of diaphragm infiltrated by tumor

gastric pain accentuated by food and relieved by emesis. There was some loss of weight. Because of these symptoms in December, 1943, a gastro-intestinal series was done at the out-patient service of an overseas hospital, with indefinite findings of a small deformity on the greater curvature near the cardia. Gastroscopy showed a patch of atrophic gastritis, and at 1500 in the antrum, a peculiar pouch giving the impression of being pulled transversely. A second gastro-intestinal series March 30, 1944, was reported as negative. Because of continued symptoms, he was admitted to a hospital overseas on April 20, 1944. Physical examination there showed nothing re-

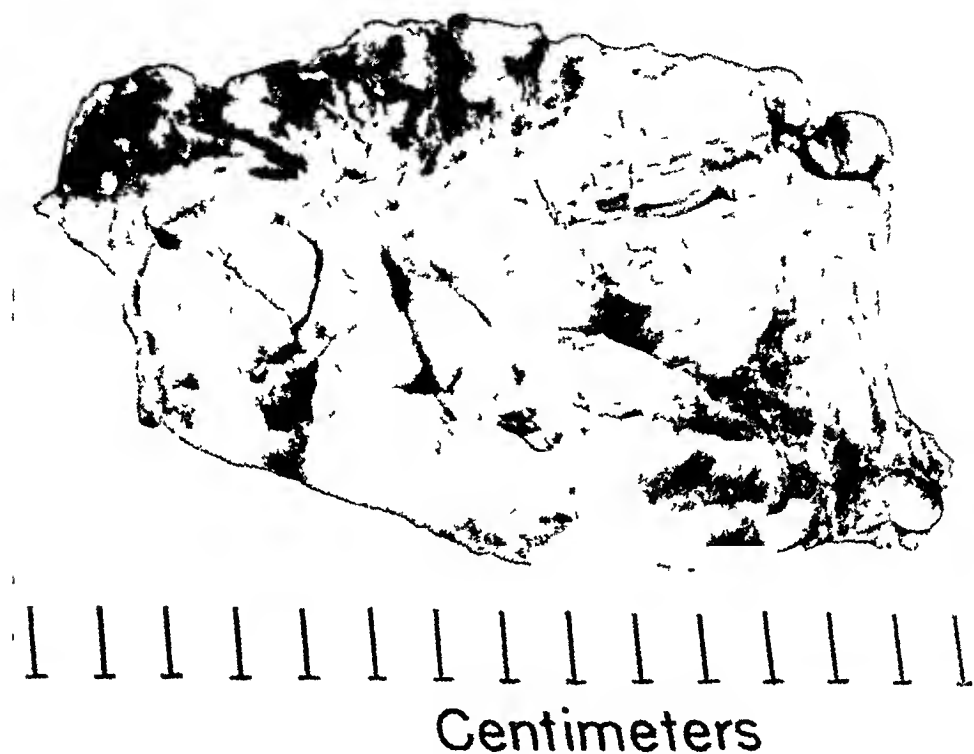


Fig 6—Case 1. Mucosal surface of stomach showing three distinct infiltrating masses of tumor with ulceration of the overlying mucosa.

markable except tenderness in the epigastrium without palpable mass. Gastric analysis showed complete achlorhydria and gastro-intestinal series showed what was considered to be carcinoma, moderately advanced, inoperable, involving cardiac portion of the stomach.

He was transferred to Walter Reed General Hospital May 8, 1944. Physical examination showed evidence of considerable weight loss. There was slight tenderness to the right of the umbilicus and in the epigastrium, but no abdominal masses were felt. Examination was otherwise essentially normal. Fluoroscopic examination May 9, showed what appeared to be an ulcerative carcinoma of the cardiac end of the stomach (Fig 1). Usual laboratory examinations were within normal limits. On May 19, he vomited a small amount of blood.

Operation—May 22, 1944. Incision was made over and parallel to the left 10th rib and the rib resected subperiosteally from the angle to the costal margin (Fig 2). The pleura was opened and the left lung collapsed. There were a few shotty calcified lymph nodes in the mediastinum. The tumor of the stomach had invaded the diaphragm over an area of about one inch in diameter (Fig 3), but there was no gross penetration of the upper surface of the diaphragm. Except for the tumor in the fundus, the stomach was free and there were no palpable lymph nodes. The incision in the diaphragm was continued as an ellipse well around the infiltrated area and back to the esophageal hiatus.

Lower esophagus and upper portion of the stomach were dissected free and the spleen removed to increase exposure. As dissection progressed it could be seen that the tumor did not quite involve the cardia but was confined to the fundus on the greater curvature. Gastric vessels were identified and exposed close to the celiac axis where they were ligated and divided. After freeing both curvatures of the stomach, stomach was transected with the cautery between clamps at about the midportion. Dissection was carried upward behind the stomach and a portion of the left lobe of the liver, which was adherent to the

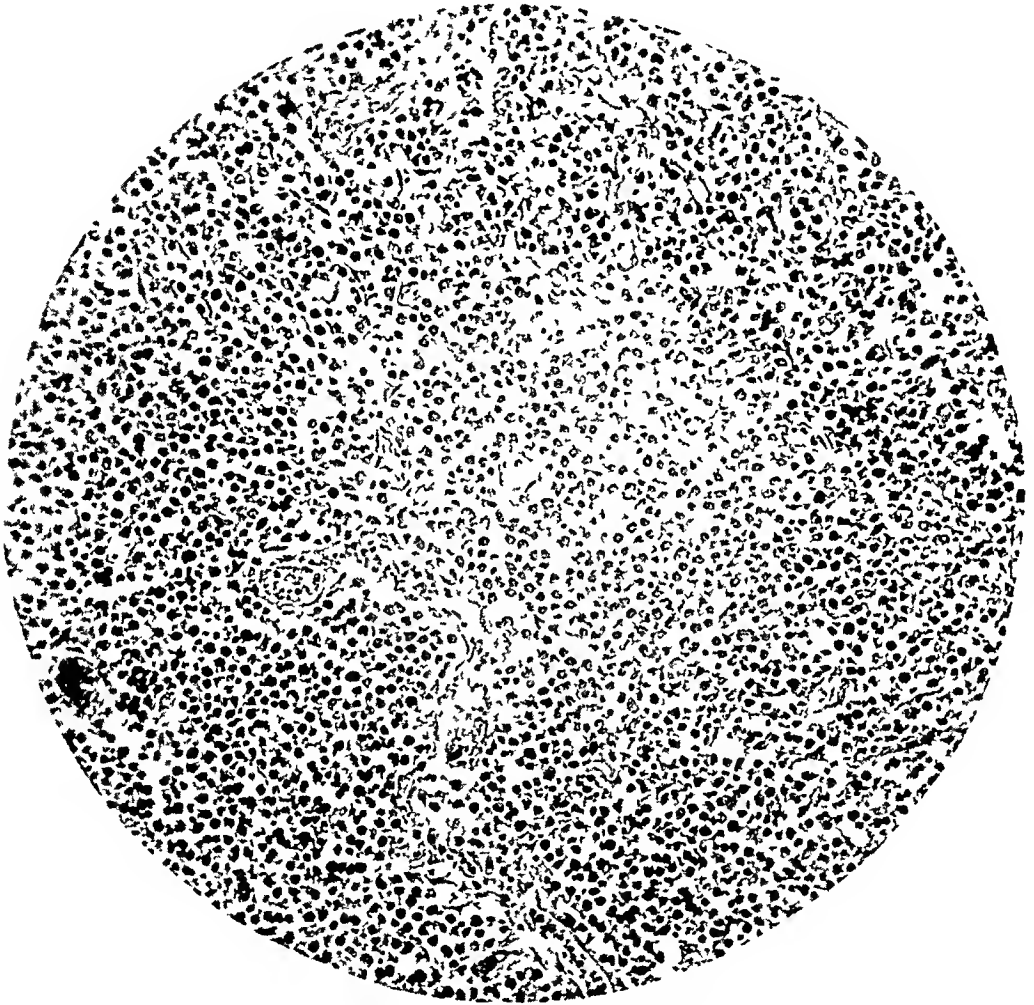


FIG 7—Case 1 Section through tumor showing the loose distribution of the cells in a fine reticular stroma which is quite vascular

tumor, was excised. As the dissection progressed it was evident that it would be possible to save a cuff of the normal stomach at the cardia from one-quarter to one inch wide (In view of the later course, this was probably an error). Incision was made along this line and the intervening portion of stomach removed. An end-to-end anastomosis was carried out between the distal portion of the stomach and the stump at the cardia. A good firm anastomosis resulted and the line of anastomosis was protected by omentum. The diaphragm was sutured above the anastomosis. Two and one-half grams of sulfanilamide had been placed in the abdomen before closure of the diaphragm, and another two and one-half grams placed in the pleura. The lung was reexpanded and the thoracic wall closed in layers without drainage.

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Postoperative course was somewhat slow. The incision healed well. Bloody, serous fluid was aspirated from the left thorax on three occasions. On July 3 roentgenotherapy was started. He received 20 treatments with the one million volt machine, for a total dose of 4,000 r to the anterior epigastrium and 4,000 r to the posterior epigastrium. About mid-August he developed severe pain in the region of the operative procedure along the distribution of the 11th intercostal nerve. This was thought to be due to trauma from retractors used to hold the wound in apposition during suturing. This nerve was sectioned September 11 with some relief. Esophagoscopy September 8 showed a wide open anastomosis with no abnormalities. Patient still complained of pain in back, sleeplessness, restlessness, and anorexia. Roentgenograms showed no metastases to

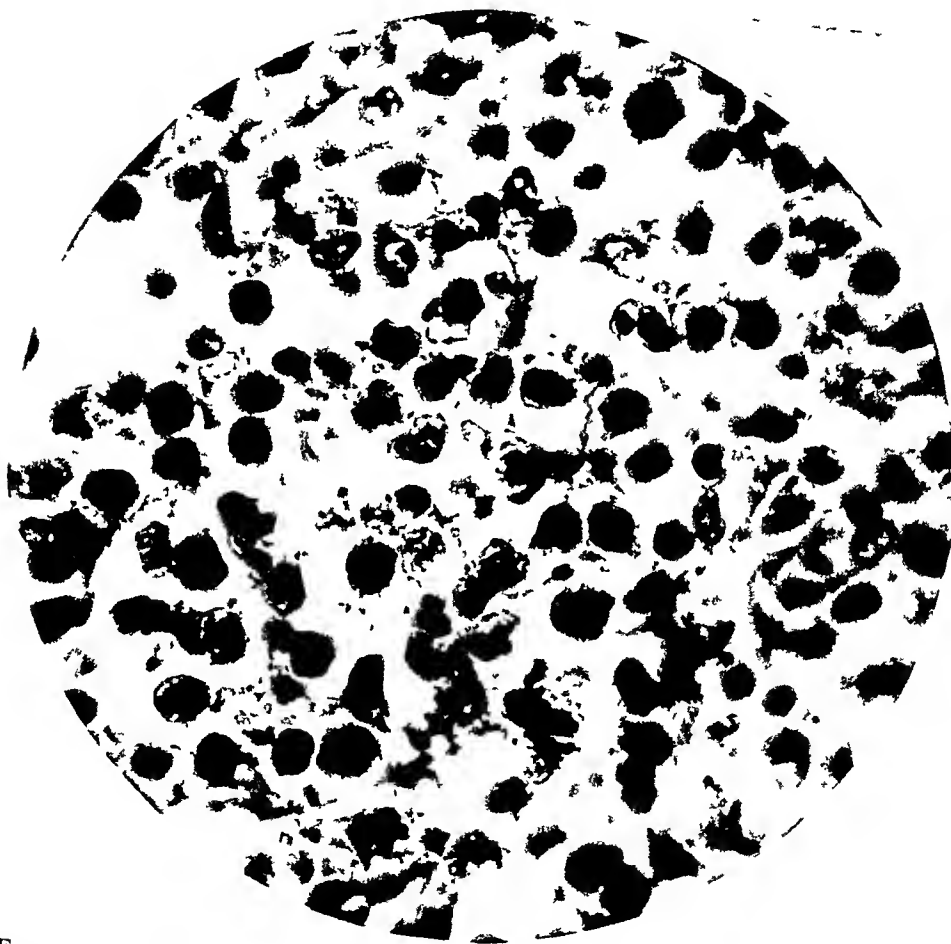


FIG 8—Case 1. Oil immersion showing typical neoplastic reticulum cells. Note the pleomorphic tendency of the deeply staining nuclei and the irregular somewhat frayed cytoplasm. A fine reticular structure is seen in this routine H & E preparation.

lungs, bones of thorax, spine, or pelvis. Barium passed freely through lower esophagus into stomach and emptied readily into duodenum. Cardiac portion of stomach appeared normal (Fig 4). About one month after discharge from the hospital, October 25, 1944, he entered a large civilian clinic because of the pain. Exploration of the mediastinum in November, 1944, at that clinic showed metastatic tumor in the mediastinum.

Pathologic Report—Capt William S. Randall, MC. Spleen weighs 115 grams and grossly shows nothing of note. Segment of stomach representing the cardia measures 10 cm long x 6 cm deep. On the posterior surface there is a 6 x 5 cm diamond-shaped portion of diaphragm centrally showing a smooth circumscribed, 2.5 cm diameter nodule of infiltrating tumor which on section is smooth, grayish-white and glistening (Fig 5). This tumor extends through the wall of the stomach and on the mucosal surface there

is a 5 x 4 cm elevated tumor centrally showing a 2 cm zone of ulceration and necrosis. On the opposite wall there is a 2.5 cm elevated mass covered with exudate, beneath which the tissues are firm, fairly moist and grayish-white (Fig 6). The surrounding mucosa is markedly edematous. One small soft node is found in the attached omentum.

Microscopic—Sections through the ulceration in the stomach reveal complete loss of mucosa and throughout the wall there is a diffuse infiltration of indiscriminately arranged neoplastic cells which show moderate variation in size and shape, but generally round to slightly ovoid (Figs 7 and 8). The nuclei are quite large, round, and the chromatin is coarsely distributed throughout. In some of the nuclei there is massing of the chromatin around the periphery simulating the nuclear structure of plasmoblasts. Throughout quite a few mitotic figures are noted. There is no stroma and between the cells there is a considerable amount of debris. There are many newly formed blood vessels, particularly over the superficial portion of the tumor. Section through the diaphragm shows widespread neoplastic infiltration and over one surface there is a marked serosal reaction. By means of the Wilder's stain a moderate amount of reticulum is noted which is in intimate relationship to the neoplastic cells. The spleen shows no significant change. One small lymph node found in the omentum reveals no alteration in the architecture.

Pathologic Diagnosis Reticulum cell sarcoma, primary, in stomach

Due to the close similarity of many of the cells to immature plasma forms, the possibility of a plasma cell tumor was considered, however, the predominant cell seems to be of the reticulum type.

Case 2—Register No 213780 White, male, age 27

Family history essentially negative except for death of father following operation for ulcer. Past history Appendicectomy for acute appendicitis in 1934. Occasional use of alcohol, no tobacco. Present illness Patient stated he had been subject to dizzy spells and vomiting all his life. About 1941 he noted abdominal distress with sense of fullness, usually coming on after eating too much or too fast. This was relieved by soda or milk. There was no hematemesis or tarry stools. He controlled the discomfort by diet fairly well until a year previous to admission, when pain in abdomen became persistent after meals with radiation to left upper quadrant. He was admitted to a station hospital on April 20, 1944, because of vomiting of blood and tarry stools. There had been weight loss of about 10 pounds in the previous six months. Roentgenologic examination on April 25, 1944, showed a large extramucosal tumor 6 cm in diameter along the medial wall in the cardiac portion of stomach, without ulceration or other abnormalities noted (Fig 9).

He was admitted to Walter Reed General Hospital on May 12, 1944. Abdomen was soft with no enlarged organs or masses palpable except for slight, indefinite fullness in upper abdomen. Remainder of physical examination essentially negative. A roentgenogram of the stomach December 14, 1943 (taken during basic training) showed indefinite evidence of a tumor at the cardiac end of the stomach measuring about 2.5 cm. Gastric analysis showed free hydrochloric acid of 20-25-25-0-20. Stools were negative for occult blood. Urinalysis normal, Kahn negative. Initial blood count within normal limits.

Operation—May 25, 1944 Thorax opened through bed of left 10th rib. No tumor could be felt in the mediastinum and although the abdominal tumor was palpable through the diaphragm, there was no invasion of the diaphragm. The tumor in the fundus of the stomach was freely movable, located just to the left and behind the cardia, involving the cardia. There were no apparent metastases in the abdomen. Lower portion of the esophagus was freed and the spleen was removed to increase exposure. Stomach was mobilized and the gastric vessels divided close to the celiac axis. The lesser and greater curvatures of the stomach were freed at about the midportion and the stomach transected and the distal end closed. Dissection was carried upward mobilizing the stomach and distal esophagus. Since the tumor involved the cardia, clamps were placed across the



FIG 9—Case 2 Tumor near cardia on posteromedial portion of stomach

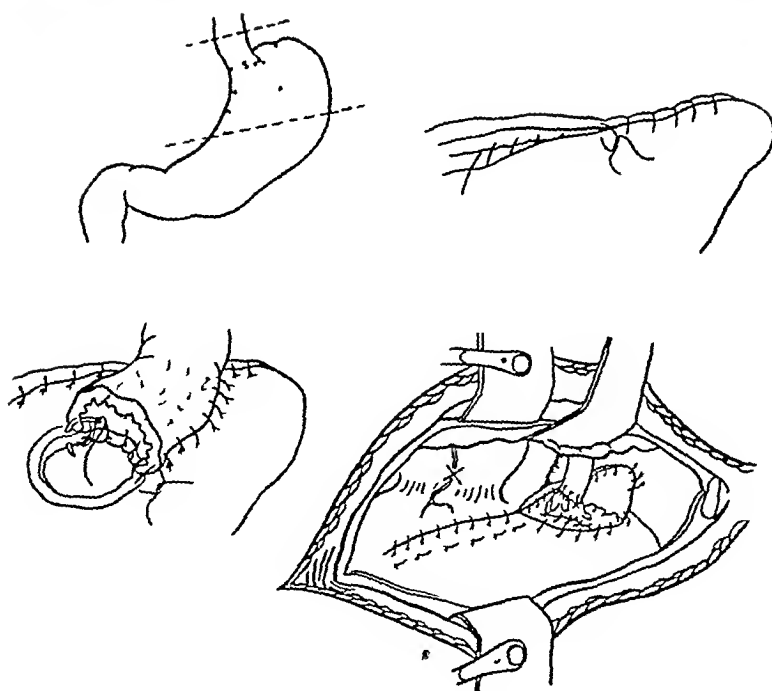


FIG 10—Case 2—Upper left Diagram of tumor and lines of resection Upper right Closure of stomach Lower left Fixation of esophagus to stomach and anastomosis Dotted lines show posterior sutures to relieve tension on anastomosis Lower right Fixation of stomach to chest wall and closure of diaphragm about stomach, with anastomosis reinforced by omentum

esophagus above the cardia and the esophagus divided between them with the cautery, removing the upper portion of the stomach and the distal esophagus. This portion of the stomach could be easily brought up into the chest so that the esophageal stump overlapped it without tension. A few silk sutures were taken to tack stomach to the posterior endothoracic fascia. The stump of the esophagus was applied to the anterior surface of the stomach. An opening was made in the stomach and the open end of the esophagus sutured into it. This anastomosis was reinforced by a tab of fat from the omentum of the greater curvature (Fig 10). Two and one-half grams of sulfanilamide were placed in the abdomen and the diaphragm was closed. Another two and one-half grams of sulfanilamide were placed in the pleura. The wound was closed without drainage after reexpanding the lung.



FIG 11—Case 2 Postoperative barium study showing small segment of stomach above the diaphragm

Postoperatively there was some collection of fluid and air in the left chest with dyspnea, which was relieved by aspiration. Postoperative course was uneventful. Gastrointestinal series June 20 showed an hiatus hernia (the portion of stomach sutured above the diaphragm) without obstruction to the passage of barium (Fig 11). Esophagoscopy August 16 showed scar of previous surgery without constriction, tumor masses, or other pathology. At the time of discharge from the hospital, October 11, 1944, he had gained considerable weight and was eating well without pain or nausea.

Pathologic Report—Capt William S. Randall, M C. Specimen consists of normal spleen weighing 80 grams. There is a portion of stomach and 1.5–2 cm distal esophagus segment. There is a bulging tumor, 6 × 4.5 cm, in the posterior wall which has infiltrated through the mucosa (Fig 12). The tumor, on section, is quite soft and friable and has a papillomatous-like structure. There are a few small superficial ulcerations at the cardioesophageal junction. The tumor bulges the mucosa and

causes almost complete obstruction to the esophagus (Fig 13).

Microscopic Section through the tumor shows widespread replacement of the wall by loosely and compactly arranged spindle-shaped cells which have a moderately fasciculated distribution. The nuclei vary from hyperchromatic to vesicular, some of the latter being quite large with small eccentrically placed nucleoli. Throughout there are fairly frequent mitotic figures without bizarre forms. There is considerable myxomatous-like degeneration in some parts and here there are a few scattered multinucleated tumor cells, these being cut transversely and having a polygonal shape. In one section there is an infiltration into the submucosa with loss of the overlying mucosa which is replaced by a zone of inflammation and granulation (Fig 14). Throughout there are many thin-walled, markedly dilated blood vessels and scattered small vascular structures, around which the neoplastic cells are radially arranged, forming structures resembling pseudorosettes (Fig 15). Section of the spleen shows nothing remarkable. *Pathologic Diagnosis* Leiomyoma of stomach wall showing low grade malignant changes.

Case 3—Register No 219413. Colored, male, age 32.

Family history negative insofar as is known. Past history irrelevant. Present ill-

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FIG 12—Case 2 Outer surface of stomach with bulging tumor which has not infiltrated the serosa



FIG 13—Case 2 Mucosal surface with tumor sectioned, occupying the entire wall. Note the white streaked appearance of the tumor

ness Patient first noticed difficulty in swallowing solid food about December, 1943, but did not enter the hospital until August 5, 1944 at which time he complained of pain and vomiting after meals for a period of three months, gradually becoming worse with intolerance to heavy foods, and a persistent feeling of retrosternal heaviness There has been a loss of about 13 pounds in weight, but no hematemesis or melena Gastric analysis showed no free hydrochloric acid Stools were positive for occult blood Roentgenologic examination August 14, showed obstructive deformity at lower aspect

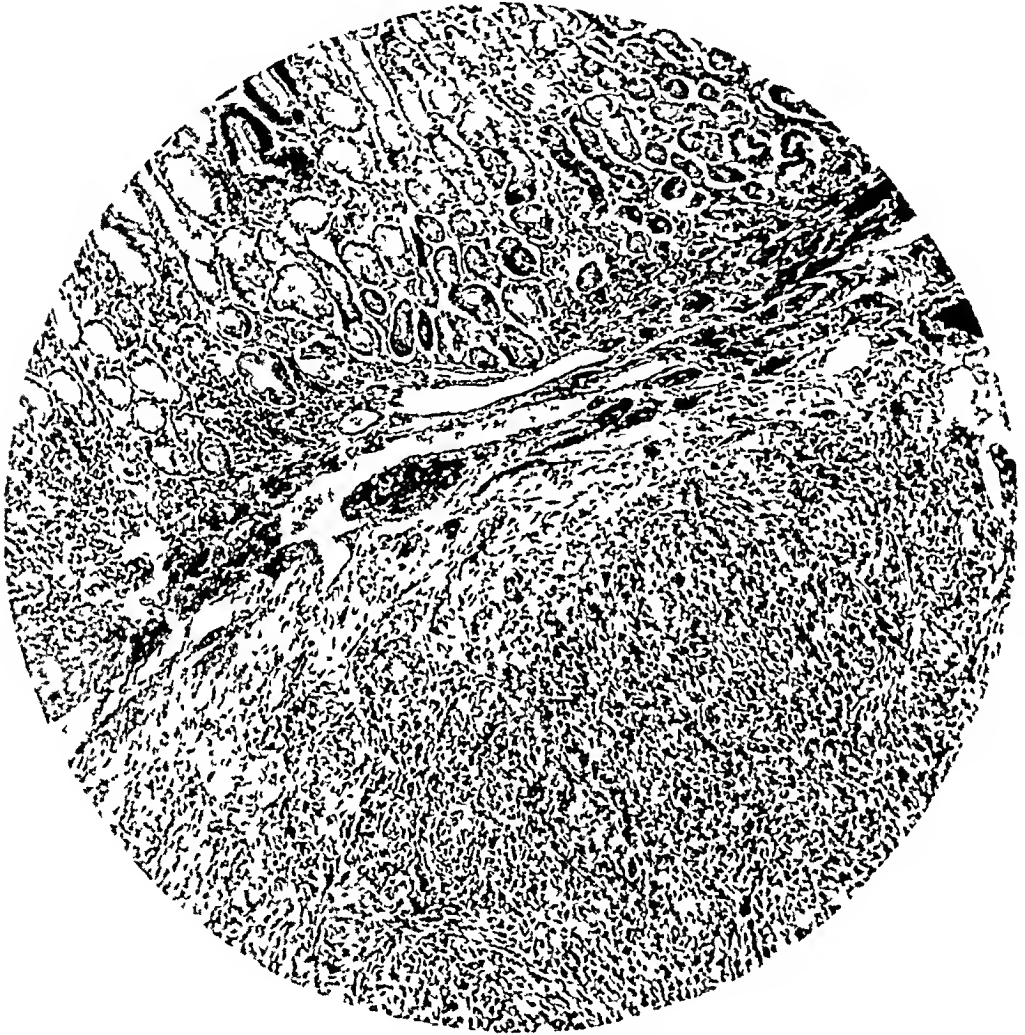


FIG 14—Case 2 Section showing submucosal distribution of the tumor

of esophagus with canalization Esophagus proximal to lesion was moderately dilated and there was a large filling defect in the region of the cardiac orifice

He was transferred to Walter Reed General Hospital September 6, 1944 At this time he had lost 25 pounds in weight since December, 1943 Physical examination was essentially negative Esophagoscopy September 11 showed the esophagus to be normal down to a point about 15 inches from the cardia where lumen of the esophagus was almost completely filled with grayish, fungating tumor tissue, springing mainly from the anterior and left lateral walls Movement of the esophageal walls at the tumor level was not obstructed and there did not appear to be any fixation Remaining lumen

was too small to admit the esophagoscope. Biopsy taken showed the esophageal mucosa to be partially intact and there was an occasional nest of cardio-esophageal glands. The stroma in most of the fragments was replaced by papillary adenocarcinoma, the cells of which were of the columnar type with granular cytoplasm and round to ovoid basophilic to vesicular nuclei which showed fairly frequent mitoses. The cells showed no significant secretion. Surrounding these zones of neoplasia there was a diffuse chronic inflammatory reaction. *Pathologic Diagnosis* Adenocarcinoma of esophagus. A roentgenogram on September 7th showed irregular annular constriction of lower end of esophagus characteristic of ulcerative carcinoma (Fig 16). Urinalysis and Kahn, negative.

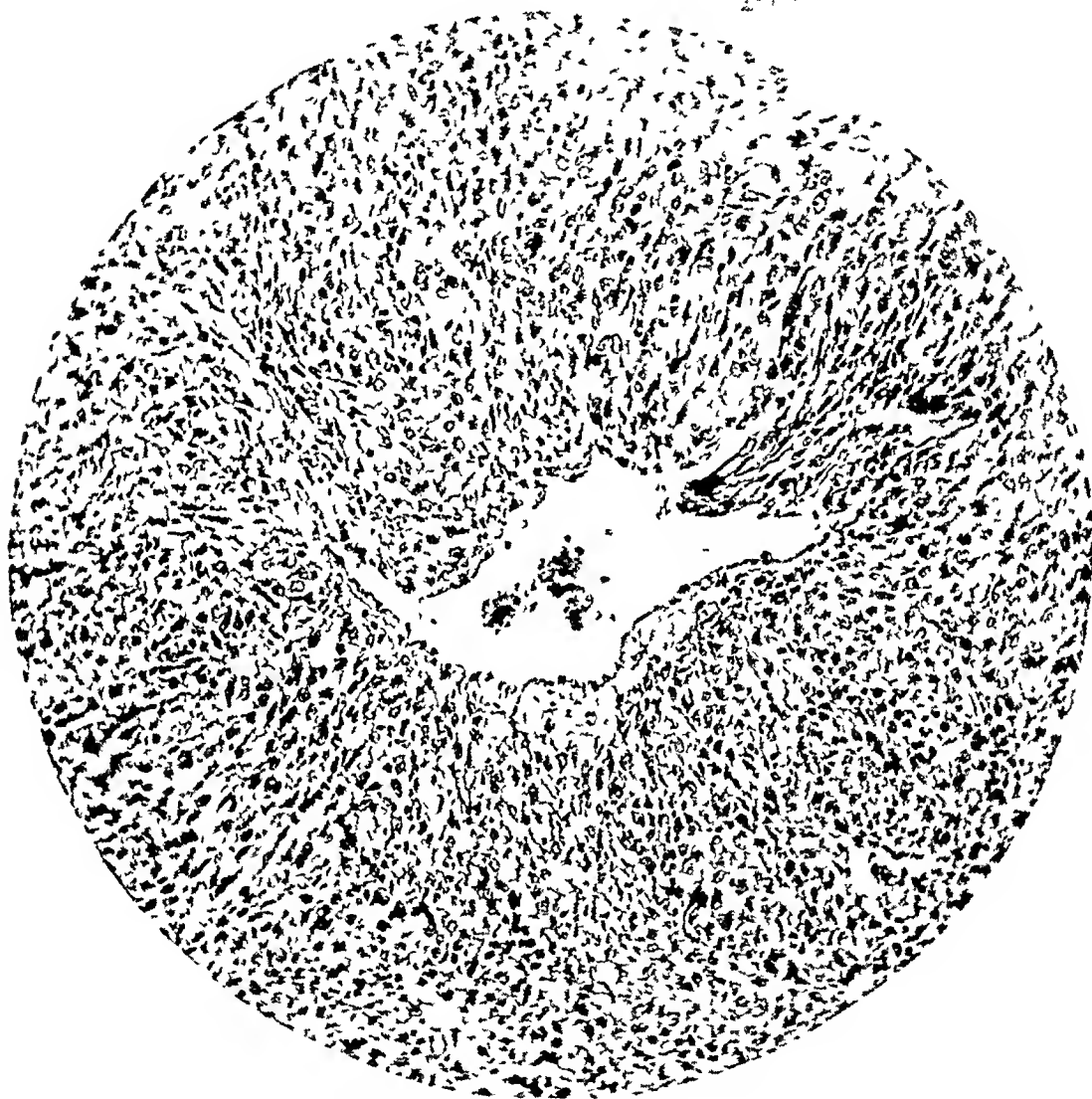


FIG 15—Case 2. Typical distribution around newly formed blood vessel. The neoplastic cells here show considerable vacuolation and centrally located vesicular nuclei are quite evident.

Operation—September 18, 1944. The thorax was opened through bed of left 8th rib. Tumor of the lower 15 inches of the esophagus was palpable above the diaphragm and tumor of the cardia palpable through the diaphragm. There were no apparent metastatic lymph nodes in the mediastinum. Tumor was found to involve the cardia and fundus of the stomach. There was involvement of the diaphragm at the cardia. Crura of the diaphragm were divided well away from the mass back to the aorta, freeing the portion of diaphragm attached to the esophagus (Fig 17). Incision was made over the esophagus up to the level of the pulmonary vein and the esophagus freed by sharp and

blunt dissection downward to the cardia. The spleen was removed for better exposure. Greater curvature of the stomach was fixed and the lesser peritoneal cavity opened. The posterior surface of this cavity was found to be involved by infiltrating tumor so that the posterior peritoneum was dissected free down to the upper margin of the



FIG. 16—Case 3. Roentgenogram showing obstruction of lower esophagus with extension of tumor into stomach.

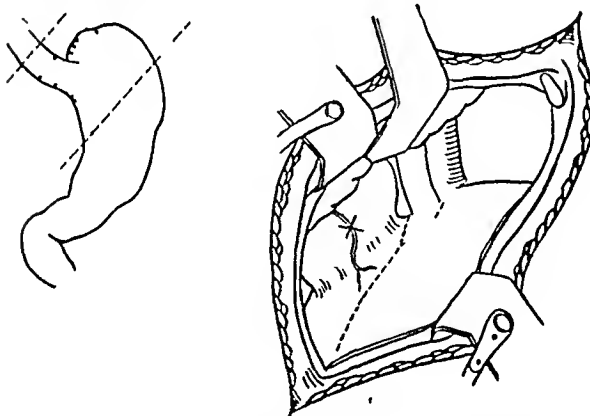


FIG. 17—Case 3—Upper left. Diagram of tumor and lines of resection. Lower right. Line of incision in diaphragm with resection of diaphragm about the esophagus.

pancreas. Left gastric vessels were ligated close to the celiac axis retroperitoneally. Frozen section of tissue taken from region of celiac axis just at the upper border of the pancreas was reported as carcinoma. The stomach was divided at about its mid-portion. Esophagus was then divided about one inch above the tumor. The proximal end of the stomach was closed with two layers of inverting silk sutures, stomach was drawn up into the thorax and the apex of the greater curvature fixed to the endo-thoracic fascia with silk sutures. Posterior surface of the esophagus was sutured to

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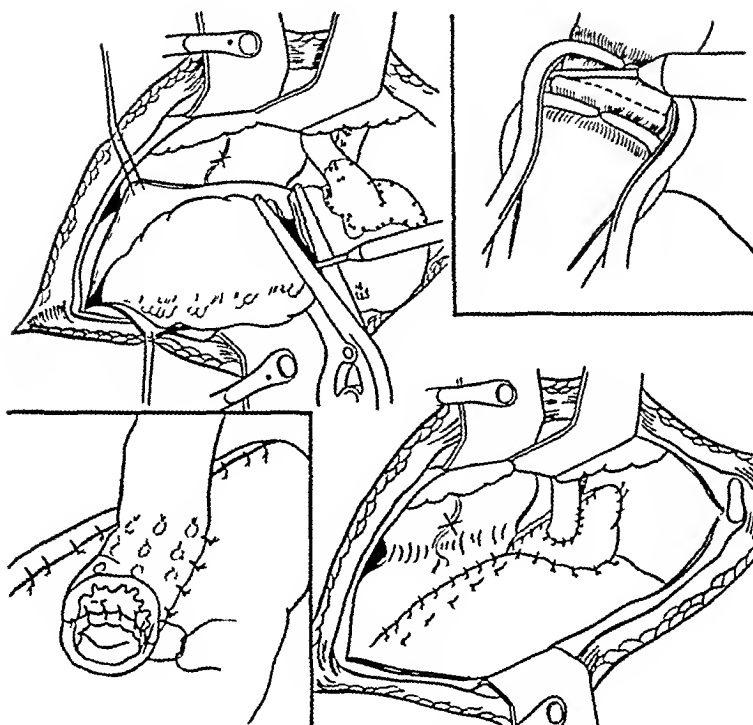


FIG 18—Case 3 Upper left Division of stomach with cautery Upper right Division of esophagus with cautery Lower left Fixation of stomach and esophagus, and anastomosis Lower right Fixation of stomach and closure of diaphragm about stomach



FIG 19—Case 3 Postoperative roentgenogram showing large portion of stomach above the diaphragm (indicated by dotted lines)

the anterior surface of the stomach for a distance of one inch. A one-inch incision was then made in the stomach and end-to-side anastomosis carried out between the esophagus and stomach. Diaphragm was closed with interrupted sutures of silk and the edges of

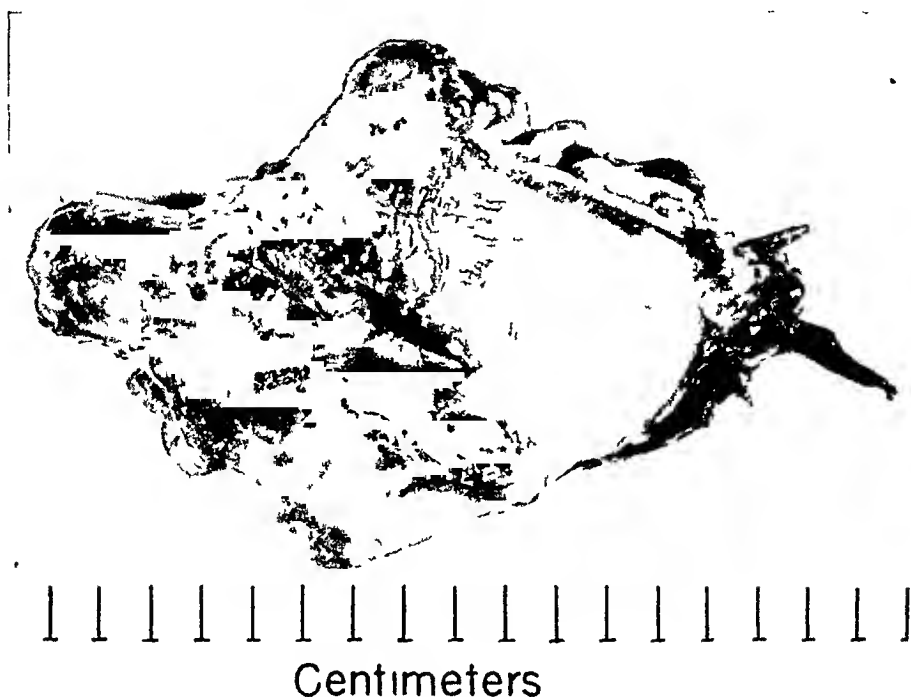


FIG 20—Case 3 Posterior view of specimen showing involved lymph nodes around the cardioesophageal junction

the diaphragm sutured to the stomach (Fig 18). Fifty thousand units of penicillin were placed in the opening of the mediastinum. Lung was reexpanded by the anesthetist and the thoracic wall closed in layers without drainage.

Postoperative course was excellent. One aspiration of bloody serous fluid in the

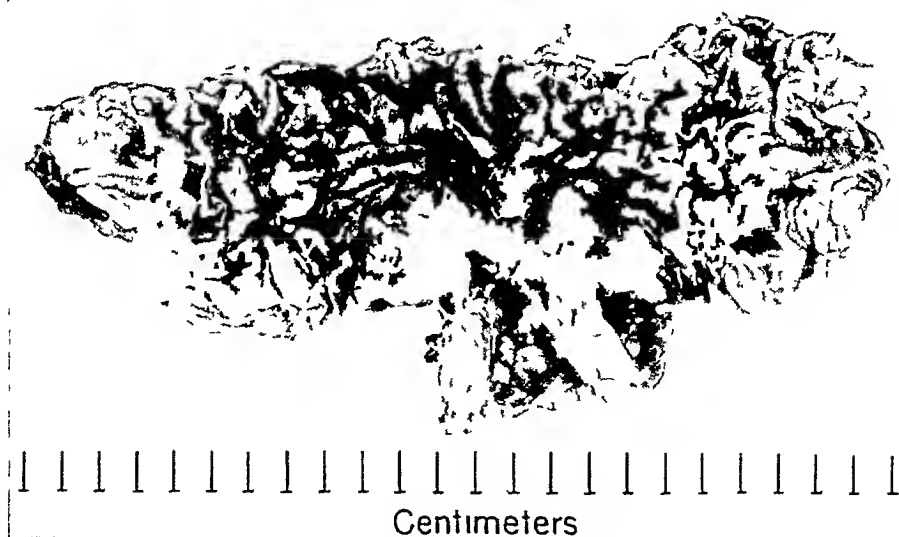


FIG 21—Case 3 Specimen opened showing greatly thickened esophageal wall with extension of the tumor into the cardia of the stomach. There is almost complete obstruction of the esophagus.

left chest was necessary. On October 20, esophagoscope was passed without difficulty. There were no signs of recurrence of tumor. Line of suture was seen where lumen was somewhat narrowed. There were no clinical symptoms of stricture and patient was eating normal diet without difficulty. At the time of his discharge from the hospital, November 8, 1944, he had gained considerable weight, was eating well, and had no

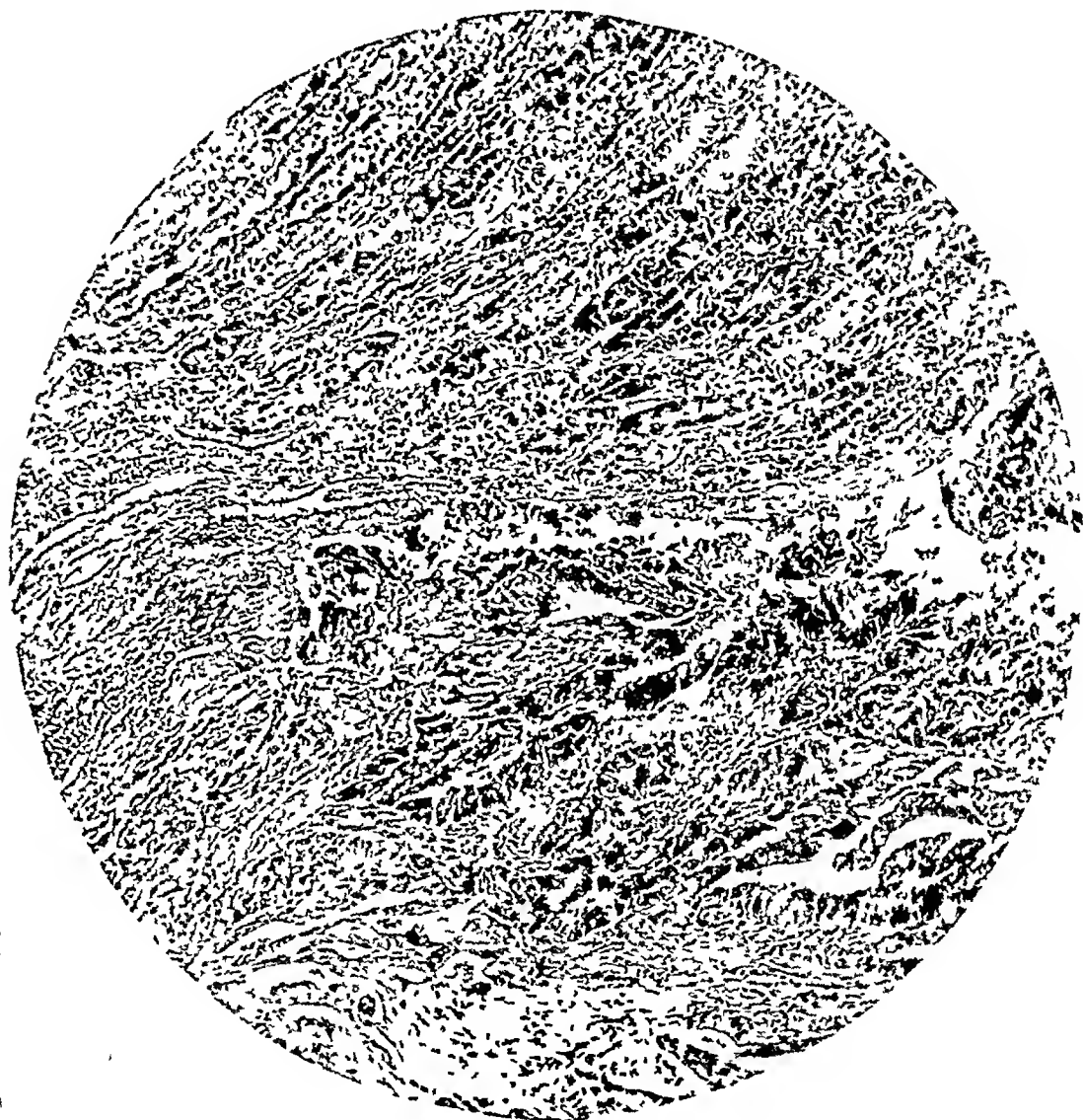


FIG 22—Case 3. Section of stomach showing extensive submucosal infiltration of the tumor.

symptoms. Fluoroscopic and film study of the esophagus and the stomach with barium swallowing, November 9, 1944, demonstrated no obstruction or filling defects. The left side of the diaphragm was located at the midportion of the stomach and did not move with respiration. Its lateral anterior and posterior portions were demonstrated and the opening for the stomach appeared adequate (Fig 19).

Pathologic Report—Capt William S. Randall, M.C. Normal spleen weighing 105 grams, which on section shows nothing of significance. With the spleen there is a 2.5 x 0.5 cm soft lymph node, showing nothing of note on section. A separate specimen consists of 4 cm of distal esophagus with a 9-cm segment of stomach. A small portion of diaphragm is attached at the cardio-esophageal junction. Around the posterior portion of the specimen at the cardio-esophageal junction there are several small lymph nodes which are quite firm and seem to be replaced by tumor (Fig 20). There is no evidence

of tumor along the resected esophageal portion or along the edges of the stomach. There is marked narrowing of the esophagus, particularly at the junction, the lumen measuring approximately 0.5 cm. Upon opening there is an 8-Mm uninvolved portion of esophagus above the tumor and at one point a 1 x 0.5 cm varix. The wall of the esophagus is 10-13 Mm thick and the tumor is firm, fairly polypoid and extends mostly along the lesser curvature for 3 cm while near the cardio-esophageal junction it almost encircles the lumen (Fig. 21).



FIG. 23—Case 3 Section taken at cardio esophageal junction showing large neoplastic glandular structures encroaching upon the "normal" esophageal mucosa.

Microscopic Section through the esophageal portion of the specimen reveals a fairly large margin of uninvolved mucosa and muscularis. The portion of the involved esophagus shows extensive replacement of the submucosa and muscularis by infiltrating strands and nests of moderately differentiated glandular structures. The glands are lined with a stratified layer of columnar cells, the nuclei of which are generally round and moderately vesicular. A few mitotic figures are noted. There is a small amount of secretion within the lumen of the glandular structures. The general histology seems to indicate primary origin in the cardio-esophageal glands. Section of the stomach shows widespread submucosal infiltration of the tumor which involves a considerable

portion of the muscular coats (Figs 22 and 23) There is rather diffuse dense fibrous reaction and here there is moderate chronic inflammation Two of the several lymph nodes around the cardio-esophageal area show secondary adenocarcinoma, one of these being completely replaced The spleen shows nothing of significance *Pathologic Diagnoses* Moderately differentiated adenocarcinoma arising in cardio-esophageal glands Secondary adenocarcinoma in regional lymph nodes Normal spleen

CONCLUSIONS

1 The transthoracic approach to the upper abdomen widens the horizons of the surgery of gastric malignancy

2 Three cases of transthoracic gastrectomy are reported, in one of which the cardia was anastomosed to the stump of the stomach, and in the other two esophagogastrostomy was carried out

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A PLAN FOR THE SURGICAL MANAGEMENT OF GASTROJEJUNOCOLIC FISTULA¹

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GASTROJEJUNOCOLIC FISTULA is a serious complication of peptic ulcer because the presence of such a communication between the stomach, jejunum and colon so profoundly influences the nutrition and health of the individual affected and because the treatment involves such a complicated and hazardous surgical procedure. That the risk in operations employed to treat patients with this condition is great is illustrated by the high mortality figures in various reports in the literature. Walters and Clagett reported a mortality of 32 per cent in 50 cases in which operation was carried out at the Mayo Clinic during the years 1928 to 1937 inclusive. More recently (1941), Gray and Sharpe, from the same clinic, reported 18 postoperative deaths in 49 cases, a mortality of 36.7 per cent. Allen reported a mortality of 25 per cent in eight cases, and Wilkie, a mortality of 40 per cent in his group of operated cases. Loewy recorded a mortality of 27 per cent in a series of 63 cases.

The cause of death in most cases has been peritonitis resulting from contamination during operation or from leakage from suture lines, or shock attending an extensive technical procedure. Pulmonary complications such as pneumonia, embolism and occasionally hemorrhage, cardiac or renal failure account for other postoperative fatalities.

Our interest in this serious problem has been stimulated by the high operative mortality reported in 1935 by Lahey and Swinton, in which the immediate operative mortality was 63 per cent in eight cases. Early in 1938 Dr. Lahey suggested a two-stage operative procedure, planned, we hoped, to avoid so high an operative risk. The first patient upon whom this plan was employed was successfully operated upon by the author in April, 1938. Since that date the operative method has been employed in 14 cases, with one death (which occurred after the first stage), a mortality of 7.1 per cent. This fatality occurred in the second case in which the operation was performed, in other words, during the period of development of certain technical steps in the operation, and we now believe that it probably represented an avoidable fatality. We propose in this communication to discuss briefly certain details of the problem of gastrojejunal fistula, to outline the operative procedure employed at present in the Lahey Clinic, and to report on 14 cases in which this method was used.

Gastrojejunal fistula most commonly occurs following operation for duodenal ulcer and in the majority of cases follows posterior gastroenterostomy. In our group of 14 cases, 12 patients had had posterior gastro-

¹ Read before the Fifty-sixth Annual Session of the Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

enterostomy and two had had an insufficient gastric resection, the original operation in all instances being undertaken for duodenal ulcer. Gastrocolic communication occasionally occurs from other causes but these cases are relatively uncommon. Fistulous communication between the stomach and colon may result from ulceration of malignancies arising either in the colon or stomach, but this, too, is not a frequent occurrence. Various other causes are given in the literature, such as peritoneal abscess and tuberculosis, and Baigen, *et al*, reported one gastrocolic fistula secondary to ulcerative colitis. However, the majority of gastrocolic fistulae follow operation for duodenal ulcer and result from jejunal or gastrojejunal ulceration at the site of gastrojejunal anastomosis. Recurrent marginal ulcer always precedes the development of the fistulous communication and may occur years after the initial operation. In one case in this group (Case 13) the fistula developed 20 years after an insufficient gastric resection (Table I).

Atwater, Butt and Priestley stated that in a series of 40 cases studied, in 42 per cent the gastrojejunocolic fistula developed within a year after the original operation. In our own group of 14 cases, the interval between the initial operation and development of the fistulous communication was much longer.

Gastrojejunal or jejunal ulcer is a too frequent complication of gastro-enterostomy. Lahey and Swinton, in a study of the literature, reported a variation of incidence of 1.41 (Veibugge) to 24 per cent (Strauss). Walters reported that ulceration occurred in three to four per cent of cases following gastro-enterostomy in the Mayo Clinic, whereas gastrojejunocolic fistula occurred in 23 of 169 cases of gastrojejunal ulcer, an incidence of 13.6 per cent. Allen reported an incidence of 14 per cent in 36 cases of gastrojejunal ulcer. Lahey, in a collective review, stated that in approximately 11 per cent of gastrojejunal ulcers, gastrojejunocolic fistula develops.

In view of the high incidence of gastrojejunocolic fistula following posterior gastro-enterostomy, it is evident that certain precautions are imperative to prevent this serious complication. Gastro-enterostomy is a valuable operation, but has a limited application and should be employed only when subtotal resection is definitely contraindicated because of the age of the patient, because of poor physical condition, and in the presence of certain technical difficulties that would make gastric resection hazardous. Furthermore, if resection is undertaken for ulcer, a considerable portion of the stomach must be removed (two-thirds or three-fourths). In two cases in which resection was inadequate in this group of 14 cases, recurrent ulcer and subsequently gastrojejunocolic fistula developed. Both of these patients had a retrocolic anastomosis and the colon lay directly upon the gastrojejunal anastomosis. The majority of the cases reported have occurred after posterior resection and posterior gastro-enterostomy. It is important that when posterior gastro-enterostomy is employed, the anastomosis should be made through an opening in the mesocolon placed near the base of the mesocolon.

TABLE I
GASTROJEJUNOCOLIC FISTULA — 14 OPERATED CASES

Case	Age and Sex	Type of Operation Preceding Fistula	Period after 1st Operation Free of all Gastro-intestinal Symptoms	Duration of Symptoms Indicating Recur Ulcer	Duration of Symptoms Indicating Fistula	Symptoms Accompanying Fistula upon Admission	Operation	Result
							1st Stage	2nd Stage
1	43 M	Post gastro-enterostomy 1929	6 years	3 5 years	3 years	7-8 stools daily, undigested food in stool	Ileocolostomy 4-4-38	Resection 4-18-38
2	34 M	Exclusion type resection 3-11-35	1 5 years	2 years	1 week	Epigastric pain, nausea, vomiting, lost 15 pounds	Ileocolostomy, resection rt colon 12-28-38	Well
3	54 M	Post gastro-enterostomy Oct 1929	2 years	5 years	4 years	Epigastric pain, 10-20 stools daily, lost 20 pounds	Ileocolostomy 7-25-40	Well
4	60 M	Post gastro-enterostomy, 1925	12 years	3 years	9 months	Epigastric pain, 6-10 stools daily, lost 40 pounds	Ileocolostomy, resection rt colon, 6-2-41	Well
5	51 M	Post gastro-enterostomy, Mar 1939	6 months	7 months	2 years	Nausea, 8-10 stools daily, lost 25 pounds	Ileocolostomy 4-21-42	Well
6	29 M	Post gastro-enterostomy, 1928	7 years	7 years	6 months	Flatulence, frequent watery stools, lost 15 pounds	Ileocolostomy 7-7-42	Well
7	53 M	Post gastro-enterostomy, 1929	3 years	11 years	1 month	Flatulence pain, frequent stools	Ileocolostomy 1-7-43	Fistula healed after first stage, well
8	49 M	Post gastro-enterostomy, 1941	1 year	18 months	17 months	Pain, 7-20 stools daily, lost 30 pounds	Ileocolostomy 6-12-43	Well
9	52 M	Post gastro-enterostomy 1936	3 years	3 years	1 year	8-10 stools daily, lost 20 pounds	Ileocolostomy 12-14-43	Well
10	52 M	Post gastro-enterostomy, 1936	7 years	6 months	6 months	Epigastric pain, severe diarrhea, lost 10 pounds	Ileocolostomy 1-29-44	Well
11	47 M	Post gastro-enterostomy, 1928	12 years	3 years	1 year	Severe pain, diarrhea, lost 60 pounds, distention of abdomen	Ileocolostomy 5-29-44	Well 9-21-44, gained 21 pounds, barium enemata failed to show fistula
12	48 M	Post resection, 1939	5 years	6 months	6 weeks	Epigastric pain, severe diarrhea, lost 15 pounds	Ileocolostomy 6-9-44	Well
13	48 M	Gastro-enteros 1922 Partial resec 1924	9 years	11 years	3 months	Epigastric pain, diarrhea, weight loss	Ileocolostomy 8-2-44	Well
14	53 M	Post gastro enterostomy 1913	11 years	3 months	1 month	Flatulence, anorexia, weight loss diarrhea	Ileocolostomy 9-14-44	Well

and as far as possible from the colon. It is important to remember that evidence of increased colon irritability occurring in a patient with symptoms of recurrent ulcer indicates that the colon is adherent to the area of inflammation about the gastrojejunal anastomosis, and is evidence of impending perforation (Fig 1). Operation should be advised and carried out as early as possible to prevent the serious complication of gastrojejunocolic fistula.



FIG 1—Impending gastrocolic fistula. Note the jejunal ulcer occurring after posterior gastro-enterostomy, the transverse colon adherent at ulcer area, and perforation of colon imminent, as proven at operation.

The symptoms of gastrojejunocolic fistula are characteristic and in the majority of the cases the diagnosis can be readily established. Recurrent ulcer distress occurring after operation, either gastro-enterostomy or resection, for peptic ulcer suggests gastrojejunal ulcer. The development of diarrhea with weight loss is strongly presumptive evidence of gastrojejunocolic fistula. Pain at first may be severe and with perforation into the colon may subside but in the majority of our cases it continued as epigastric distress. A history of belching of foul gas or vomiting of foul stomach

contents may be obtained in many cases. The stools are watery, frequent (6 to 20 per day), and often contain undigested food particles. Weight loss is often extreme and in two cases was as much as 40 pounds within a few months. In addition to emaciation, dehydration, nutritional edema, hypoproteinemia, anemia and serious states of vitamin deficiencies are often encountered.

Roentgenologic examination readily confirms the clinical diagnosis. Positive roentgenographic findings were present in all of our 14 cases. The fistulous communication is usually easily visualized by barium enema (Figs 2 and 3), and under the fluoroscope the barium mixture can be seen pouring into the stomach from the colon. The diagnosis was established in the majority of our cases by roentgenologic examination after a barium enema, in four instances the fistula was first visualized following the ingestion of a barium meal (Fig 4).

The majority of gastrocolic fistulae occur in men, and in our series all patients were males. This is the experience of other writers upon this subject. Walters reported that only one patient in his group of 50 cases was a woman.

In most of the cases of gastrojejunal fistula reported by other writers, the patients were between 40 and 60 years of age. A similar age distribution is noted in our series. Only two patients were less than 40 years of age, the youngest being 29 years and the oldest, 60 years.

The treatment of gastrojejunal fistula is purely surgical and the surgical management of a large gastrojejunal fistula is technically difficult and often accompanied by considerable operative risk. The generally poor condition of these patients, the stage of malnutrition, the marked alteration in protein and blood chemistry findings make any extensive operative procedure, with measures to improve these states, entirely unsafe and, consequently, unwise. Most of these patients have had repeated abdominal operations, which have resulted in extensive adhesions and distortion of abdominal anatomy. This makes for time-consuming dissection to identify structures and establish anatomic relations before any restorative operative procedure can be carried out.

In an endeavor to avoid the high operative risk in these cases, numerous operative procedures have been suggested and employed by different surgeons. Experience has demonstrated that in order to prevent the recurrence of ulceration in any complicated ulcer case, a radical subtotal resection of the stomach should be employed and that an ulcer is less likely to recur after resection. It is evident, therefore, that in addition to excision of the fistulous tract, a radical subtotal gastrectomy should be included in the operative plan. However, an extensive block dissection of the fistulous tract in addition to a subtotal gastrectomy undertaken in one stage is entirely too hazardous to employ and would certainly result in a high percentage of fatalities. An operation designed to excise the fistulous tract and disconnect

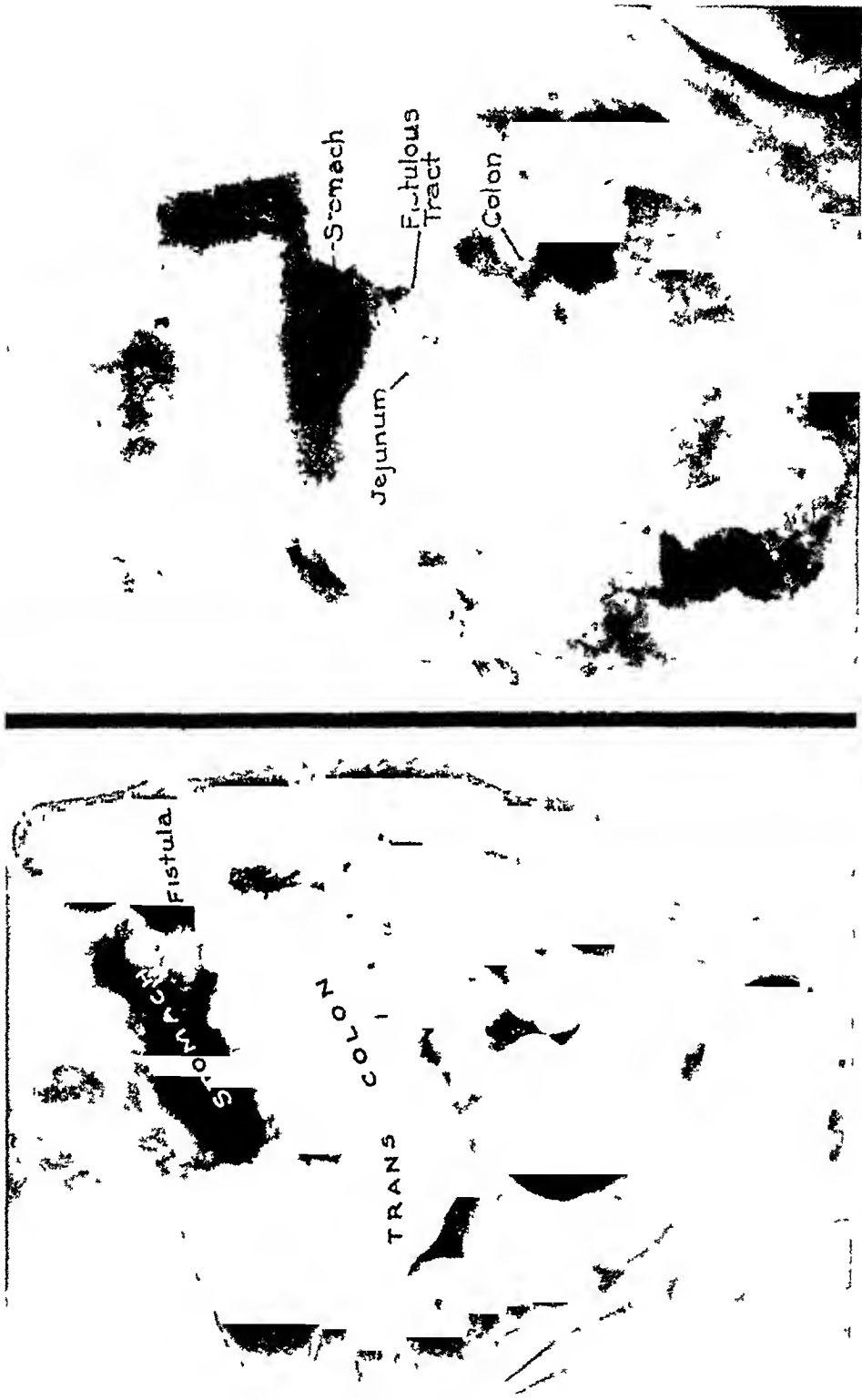


Fig 2 —Roentgenogram taken after a barium enema, demonstrating a gastrojejunal fistula. Barium sulfate, given by enema, partially fills the stomach. Note the fistulous communication and also the constricted area in the transverse colon at point of the fistula (Case 9)

Fig 3 —Gastrojejunal fistula. Barium sulfate given by enema is shown to enter the stomach and jejunum from the colon through the fistulous communication

the stomach, jejunum and colon is undoubtedly the simplest form of surgical approach, but reestablishment of normal gastro-intestinal continuity will result in recurrent ulcers in a large group of cases, and it is not to be recommended in the majority of cases. Furthermore, the induration and extent of the inflammatory exudate may preclude any possibility of closing the rent in the colon or jejunum, and disconnection may compel the surgeon to proceed with extensive resection of the involved colon and jejunum, which immediately places the operation at a high risk level.

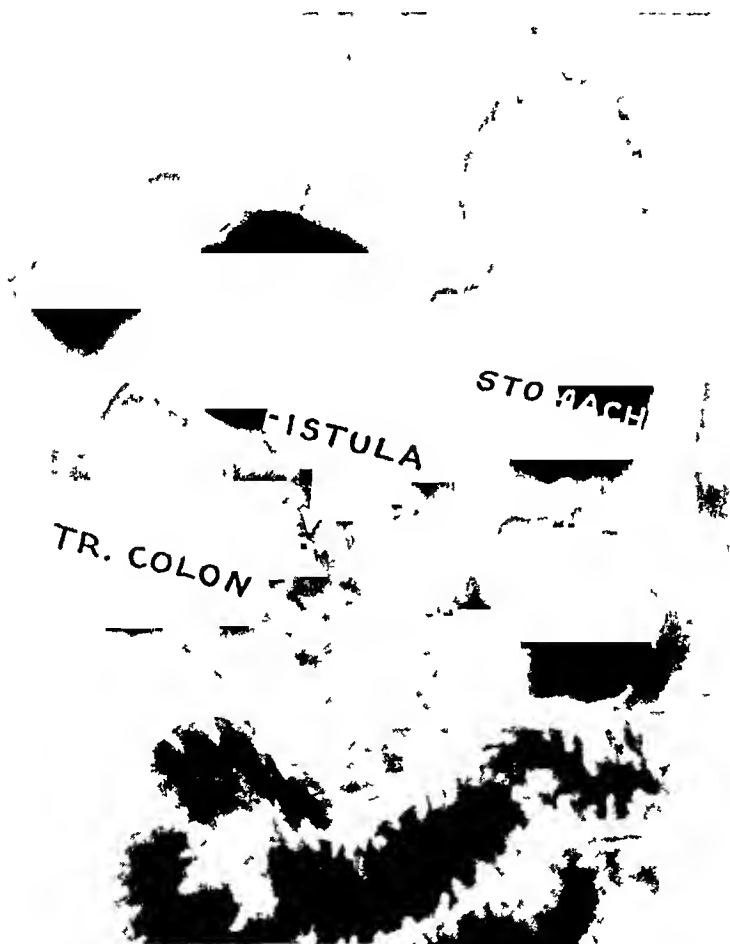


FIG. 4—Roentgenogram taken after a barium meal demonstrating a gastro jejunocolic fistula. The barium has passed readily from the stomach into the transverse colon and into the jejunum. Note the area of spasm in the colon (Case 5).

Simple excision of the fistulous tract and restoration of gastro-intestinal continuity has been most often employed in groups of cases reported and it is with this type of operation that the mortality has ranged from 25 to 63 per cent. In addition, the tendency to recurrent ulceration profoundly influences the type of operation that should be employed for gastrojejunocolic fistula and a simple disconnecting operation, therefore, is not to be recommended because of the high recurrence rate. In Walter's series of 50 cases, most patients had a simple disconnecting operation and only nine had

an additional subtotal resection, yet the mortality in this group was 32 per cent Finsterer has preferred a one-stage operation for gastrojejuno-colic fistula, but employed a two-stage operation if simple closure of the colonic fistula was impossible He reported operation in 13 cases, with five deaths, a mortality of 38.4 per cent

Because of the poor nutritional condition of patients with gastro-jejunocolic fistula and because the operation in most instances involves long and tedious dissection, a two-stage procedure is to be recommended

Pfeiffer,⁹ in May, 1938, presented before the American Surgical Association an operative method employing a preliminary colostomy proximal to the fistula as a first-stage procedure In 1941, he reported¹⁰ a series of collected cases in which this plan had been employed, ten patients had gastric resection in the second stage and five had simple excision of the fistula and restoration One death resulted in this group, a mortality of 6.6 per cent

This operation by Pfeiffer apparently reduces the operative hazard greatly and his mortality is the lowest yet reported in any operation designed to treat the serious complication of peptic ulcer This method, however, presents certain technical problems which tend to complicate the operation and are, to a certain extent, undesirable During the second stage, any extensive block dissection of the fistulous communication with additional gastric resection has to be carried out in the presence of a right colon fixed to the abdominal wall by virtue of the established colostomy and, also, in the presence of fecal contamination of the abdominal skin surface The colon fixation adds to the difficulty of mobilizing the transverse colon, duodenum and pylorus in event of gastric resection Soiling of the abdominal wall by a draining colostomy increases the hazards of abdominal wound and peritoneal infection Moreover, on completion of the second stage, whatever it may be, the surgeon still has the colostomy opening to close, which adds to the extent of operation

The operative procedure for treatment of gastrojejunocolic fistula employed at present at the Lahey Clinic, according to the plan suggested by Doctor Lahey, was first used in April, 1938 Since that date we have used this method in 14 cases, with one death, a mortality of 7.1 per cent This operative plan consists of a two-stage procedure and employs the principle of block excision of the section of jejunum and colon involved, plus gastric resection The first stage of the operation is designed to divert small intestinal and colonic contents from regurgitating into the stomach and jejunum This is accomplished readily by dividing the terminal ileum and performing an ileocolostomy between the terminal ileum and descending colon Small intestinal and right colon contents are thus emptied into the descending colon and cannot reenter the stomach and jejunum The toxic and irritating effects of such regurgitation are thus avoided, and these patients have tended to improve in nutrition, gain in weight and in most

instances have complete cessation of diarrhea. If the diarrhea does not completely cease, the number of stools per day in all cases is greatly reduced. It is important that the first stage of the operation be as simple as possible, because it is at this stage that the patient's condition is at its poorest. Our single death occurred in the second patient operated upon, and after the first stage during which the right colon was removed in addition to ileocolostomy, in

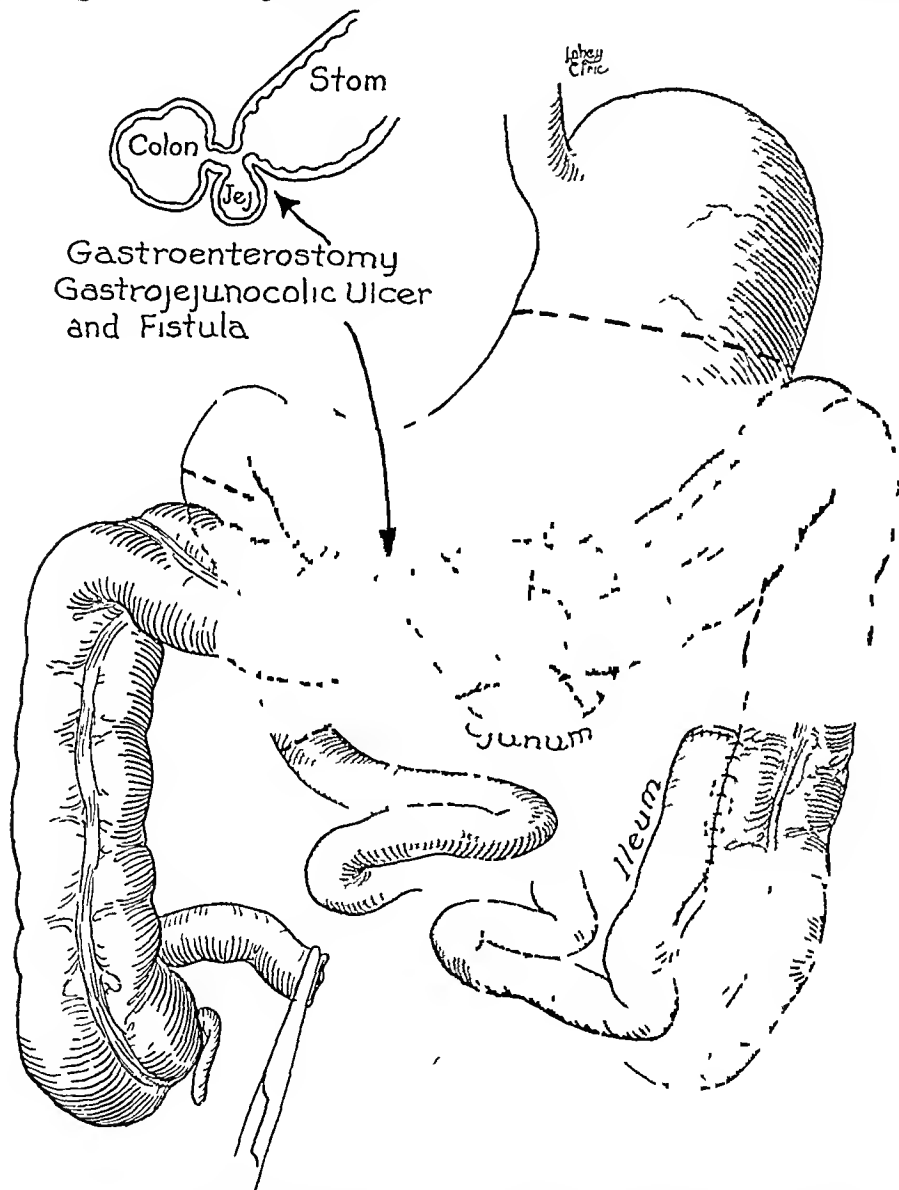


FIG 5—First stage of operation for gastrojejunocolic fistula. The terminal ileum has been divided, the proximal end of ileum has been closed by inversion and a side to side anastomosis between the terminal ileum and descending colon has been established. The distal end of divided ileum is likewise closed by inversion and dropped back into the abdomen. The light segments indicate the portions of stomach, colon and jejunum which are to be removed at the second operation.

the hope of simplifying the second stage of the operation. The right colectomy should not be undertaken during the first stage because it materially adds to the technical procedure of the first stage and increases the risk at a dangerous period of the patient's nutritional imbalance.

GASTROJEJUNOCOLIC FISTULA

The first stage of operation for gastrojejunocolic fistula (Fig 5) is as follows. The abdomen is opened through a left rectus incision. The involved areas of colon, jejunum and stomach are inspected and gently palpated, care being exercised to avoid separating adhesions in this area, which might possibly lead to leakage about the inflamed fistulous tract. The terminal ileum is identified and divided about six inches from the ileocecal valve, the mesentery being split sufficiently to permit approximation of the terminal

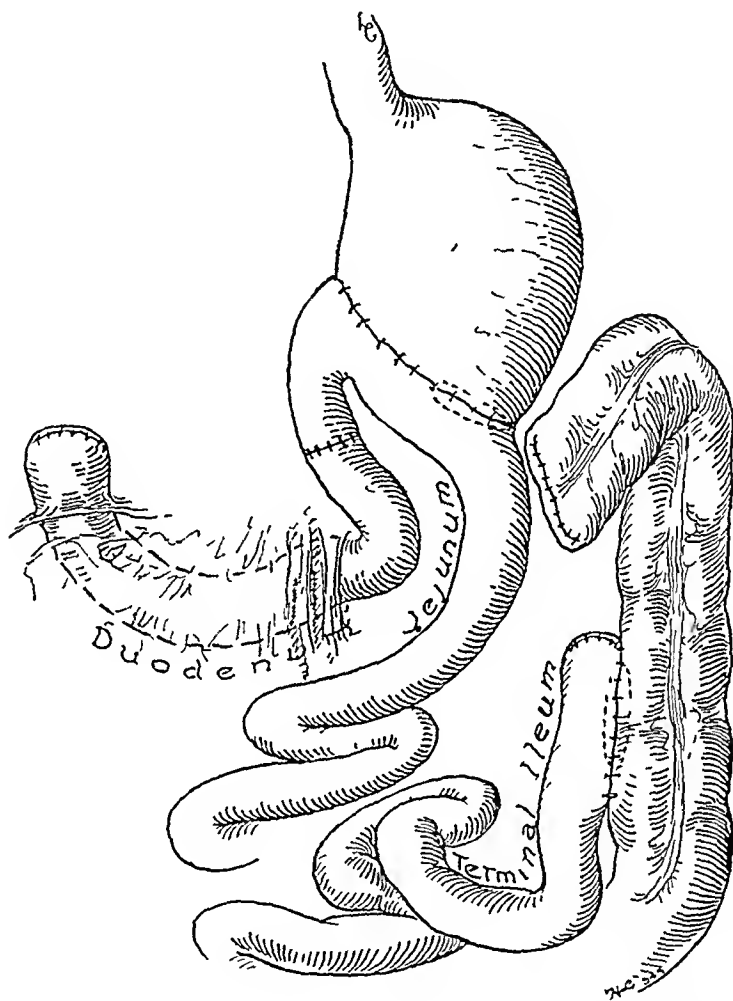


FIG 6—Second stage of operation for gastrojejunocolic fistula. Drawing illustrates the completed operation. Note that the right colon and transverse colon to a point past the fistula, together with the portion of the jejunum involved with ulcer, have been resected. A gastric resection completes the operation.

ileum to the descending colon. The divided ends of the ileum are closed by inversion with layered sutures of catgut and silk. A side-to-side anastomosis of ileum to descending colon is then established and the abdomen closed in layers.

When the method was first used, the second stage was carried out in about two weeks after the first stage. However, it early became evident that a longer interval should elapse between stages in order that the patient's nutrition and general condition could improve. It is now an established practice to send these patients home for a period of two or three months before completing the operation by the second-stage procedure. A diet high

in vitamins protein and calories is given during this interval. Marked gain in weight is usual and one patient gained as much as 40 pounds between stages. Marked improvement in general condition was noted in all cases.

The second and final stage of the operation for gastrojejunocolic fistula is as follows (Fig. 6). The abdomen is again opened through a left rectus incision which extends from the costal margin to a level below the umbilicus. The cecum, right colon and transverse colon are mobilized to a point distal to the colonic fistula. All mesenteric attachments are divided. The transverse colon beyond the fistula is then divided with the actual cautery between clamps, and the end of the distal portion of the transverse colon is inverted with catgut sutures, which are reinforced with interrupted silk sutures. The colon and attached stomach may then be turned forward and the involved loop of jejunum is readily visualized and likewise resected. A high resection of the stomach after mobilization and division of its attachment completes the block excision of the fistulous tract and involved viscera. An end-to-end jejunal anastomosis is carried out before completing the gastrojejunal anastomosis (Fig. 7). The operation is extensive, but not nearly so formidable as it would appear. Mobilization and division of the colon permits easier mobilization of the stomach and ready resection of the jejunum. All of these cases have been operated upon without shock, and the convalescence has been remarkably uneventful after such an extensive resection (Fig. 8).

Our experience with two cases has been of especial interest. One patient (Case 11), 47 years of age, who had had definite symptoms of gastrojejunocolic fistula for a period of a year, during which time he had lost 60 pounds in weight, reported immediate improvement following the first-stage operation of ileocolostomy. Four months after operation he has gained 21 pounds, diarrhea has completely ceased and he has been completely asymptomatic. Repeated examinations with barium enema have failed to show any colonic communication even though this could be readily demonstrated by barium enema before operation. Another patient (Case 7), 53 years of age, who had symptoms of gastrocolic fistula of one month's duration and who had indisputable roentgenologic evidence of fistulous communication apparently has also obtained healing following the first stage. Barium enema has failed to show colonic communication and to date, nearly two years following the first-stage procedure, he is quite well. It should be emphasized however, that the great majority of patients with gastrojejunocolic fistula will require the second-stage gastric resection and block excision of the fistulous tract in order to be completely freed of all symptoms. In view of these two cases in which the fistula closed after the first stage with marked improvement in nutrition and cessation of diarrhea and distress roentgenologic examination should again be repeated in every case before the second stage of the operative procedure is carried out. Should examination fail to reveal the colonic fistula, no harm can result from deferring the second stage provided the patient improves in health and provided repeated examinations fail to show the fistula.

GASTROJEJUNOCOLIC FISTULA

a



b



FIG 7.—Specimen, gastrojejunocolic fistula, removed at second stage of operation
(a) The colon has been opened and a large fistulous orifice into the colon is demonstrated
(b) The gastric and jejunal mucosal surfaces are shown, illustrating the site of the fistula which opens into the colon Note that a

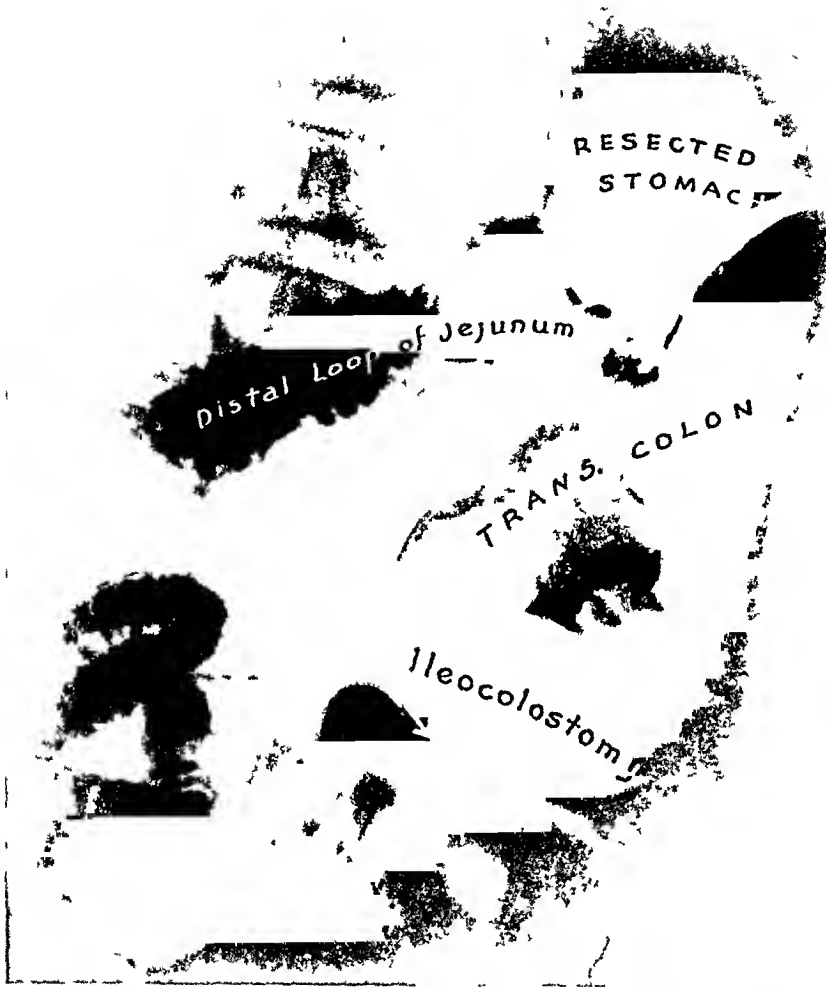


FIG 8—Roentgenogram taken after second stage operation for gastrojejunoileic fistula. Barium sulfate mixture was given by mouth and also by enema. Note the resected stomach and also the remaining colon and the anastomosis between the terminal ileum and the colon.

SUMMARY

Gastrojejunoileic fistula is a serious complication of peptic ulcer and any surgical method of treatment will require an extensive operative procedure which may be extremely hazardous.

Gastrojejunoileic fistula follows gastrojejunal ulcer and occurs in about 11 to 14 per cent of such recurrent ulcers.

Surgical treatment of this condition should consist of excision of the fistulous tract combined with a high gastric resection.

A two-stage operative procedure is to be recommended. A two-stage method employed in the Lahey Clinic is described. Results in 14 cases in which the operation has been employed are briefly reported.

The immediate operative mortality in the group of 14 patients was 71 per cent.

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DISCUSSION—DR. J. SWINTON HORSLEY, Richmond, Va Doctor Rienhoff is to be congratulated on the results he has obtained and the excellent way in which his patients have been followed

For a good many years I have been using a modification of the Billroth-I type of partial gastrectomy, which I have published several times Of course, no one type of partial gastrectomy is always applicable and I occasionally use a type of Billroth-II, as the Hofmeister or Polya, such as Doctor Rienhoff describes

Peptic ulcer of the duodenum is usually cured by medical treatment, but in the event that it cannot be so cured and it becomes a surgical case, the lesion is often in the posterior wall of the duodenum and has penetrated into the head of the pancreas At least, this has been my experience One of the chief difficulties in such cases is the treatment of the stump of the duodenum If the ulcer is removed the stump of the duodenum is short and difficult to close If a little shelf of the posterior wall of the duodenum is dissected from the pancreas, the stump of the stomach can be brought over and united to the duodenum with a series of interrupted mattress sutures of chromic catgut All of these are placed before any one is tied, and if before tying them the Payr clamp is removed from the stomach and an incision of about 1 to 1.5 inches is made in the anterior wall of the duodenum, the stomach can be puckered and a straight end-to-end anastomosis may be made Before tying these sutures, a tag of omentum is brought over the raw surface of the pancreas behind the sutures and sutured to this surface and to the upper border of the pancreas This tends to reinforce the posterior portion of the anastomosis and covers the raw surface of the pancreas The rest of the operation is performed as described elsewhere The posterior margin of

the stump of the stomach is then sutured to the posterior margin of the shelf of the duodenum with a continuous lock-stitch of chromic catgut

The value of giving proteins as soon as possible after operation is being emphasized more and more. After the posterior portion of the anastomosis has been completed, a forceps is passed through the stump of the stomach and pushed through the anterior wall of the stomach at a point about four inches from the margin of the stump. Two small catheters with additional perforations are drawn through, one for about 3.5 inches and the other for almost its entire length, leaving only about four inches of it outside the stomach. Each catheter is sutured to the gastric wall separately with fine chromic catgut and a purse-string suture is then placed around both. The short end drawn through is left in the stomach and the long end is carried through the duodenum with long forceps and into the jejunum. The anterior portion of the anastomosis is then resumed and the two catheters are brought through a stab wound to the left of the incision, or through the upper portion of the abdominal wound. The anterior wall of the stomach is sutured to the parietal peritoneum and a tag of omentum is drawn around the catheters for further protection. Thus, the stomach is kept empty without the discomfort that an indwelling nasal tube would bring, while through the other catheter a formula of proteins for the jejunum can be introduced within 48 hours after operation.

There are, to be sure, some recurrences of duodenal ulcer or anastomotic ulcer which is duodenal after this type of operation, but they usually can be treated medically with success. I have had to operate upon only one case of recurrent ulcer after this type of gastrectomy, and then I did a gastro-enterostomy, and the patient obtained perfect relief. After a Billroth-II type of operation, however, the prospect of a jejunal ulcer hangs over the patient, it may not occur for many years. And a jejunal ulcer is a very different problem from recurrent duodenal ulcer. It almost always requires a difficult and serious operation, and even then the conditions that produce a jejunal ulcer are not materially altered.

The criterion as to the presence of free hydrochloric acid in the stomach after a type of Billroth-II operation is often fallacious. The duodenal contents, in which the chief alkaline factor is pancreatic juice, may flow into the stomach to such an extent as to neutralize the free acid secreted by the remaining part of the stomach. There is, too, the natural tendency for a deficit in the function of an organ to be replaced by hypertrophy and hyperplasia of the organ. Thus, it is well known that large portions of the kidney or the liver may be experimentally removed if done at intervals, and the remaining portion will usually hypertrophy sufficiently to carry on vital function, which would not occur were too much of these organs removed at one time. This seems to be true with the stomach, after removal of large amounts, the remaining portion hypertrophies and a much more free secretion of acid in the gastric juice results. The small intestinal tract increases in sensitivity to gastric acid from the duodenum down. As physiologists have shown, there is a natural regurgitation of duodenal contents into the stomach during the normal process of digestion, and one cause of a peptic ulcer is spasm of the pyloric portion of the stomach which prevents the normal regurgitation of duodenal contents. After removal of the pyloric end of the stomach there is nothing to obstruct a full amount of regurgitation of duodenal contents.

As for gastrojejunal fistula, the cause of such a fistula is excessive hydrochloric acid in the gastric juice. This is distinctly antiseptic and renders this type of fistula quite different from an ordinary fistula in aseptic colon. Consequently, it would seem that extensive resection of the colon in such a condition is unnecessary, even though there may be some ulceration in the colon, if the irritating cause of this ulceration—high acid content of the gastric juice—is removed, the ulcer will doubtless heal.

DR R. L. SANDERS, Memphis, Tenn. I shall confine my remarks to Doctor Rienhoff's subject. I am of his opinion that a study of cases in private practice should give us an idea of where we stand after 25 years of dealing with stomach problems. With this objective, we recently made a study of our cases of gastric resection for stomach and duodenal ulcer and reported the findings at the meeting of the Western Surgical Association.

This study covered a period of 26 years (1918-1944), and included 1,218 private ulcer cases, divided into two groups, from 1918 through 1931, and from 1932 to the

GASTROJEJUNOCOLIC FISTULA

present time In the first group we did 35 pyloroplasties, 125 gastro-enterostomies and three resections In the second group there were 14 pyloroplasties, 58 gastro-enterostomies and 101 resections We have not done a pyloroplasty in five years, since 1940 the number of resections has increased 25 per cent while the number of gastro-enterostomies has diminished correspondingly At the present time, three-fourths of our operations for primary duodenal ulcer are resections Thus, during the past decade we have swung definitely from palliative to radical treatment of duodenal ulcer

We also agree with Dr Rienhoff that, if one takes out the ulcer-bearing zone, the result will be satisfactory In the average case we do not remove more than 65 per cent of the stomach With this operation we have found that 80 per cent of patients are completely relieved and an additional 10 per cent partially relieved The remainder have had symptoms and clinical evidence of recurrence, or have had some complication which has obscured the result of the operation

When one considers this partially relieved group one wonders if the pendulum has swung too far toward resection These patients no longer have intractable pain, but still have a little nausea and perhaps some vomiting, they are weak and anemic and cannot gain weight The question is even more serious concerning the unrelieved group Perhaps a gastro-enterostomy would have been the better procedure On the other hand, had a gastro-enterostomy been done, a resection might ultimately have become necessary Some patients apparently have what we call the "ulcer diathesis," and no matter what is done, either medically or surgically, they remain unchanged They are the ulcer type and, despite even radical resection, are candidates for further trouble We do not yet have the answer to the problem in these cases, but until we do it is well to remember that, although we may expect fewer recurrent ulcers after resection, gastro-enterostomy is still the best operation for a good number of patients

DR WILLARD H PARSONS, Vicksburg, Miss I desire to add three additional case reports to those presented by Colonel Griswold Each was operated upon by a trans-abdominal approach, and I am inclined to believe that general surgeons, untrained in the refinements of thoracic surgical technic, will find this approach preferable to the transthoracic route Thoracic surgeons may find the transthoracic as safe as the abdominal route, however, and in their hands such a procedure may be superior

The first patient, a woman past the age of 50, was found on study and at surgery to have a benign gastric ulcer somewhat larger than is usually encountered The case is of interest, however, because as shown (slide) there is demonstrated by tissue section one of the larger major bleeding points at the base of the ulcer A thrombotic plug in one of the major arteries is shown, and the bleeding from this vessel was controlled only by gastrectomy

The next patient, a woman, age 38, came to the Clinic because of serious gastric hemorrhage of such severity that the hemoglobin level was 40 per cent, erythrocytes 2,050,000 The roentgenograms ultimately revealed a very small prepyloric lesion Radical subtotal gastrectomy was done with inclusion of great omentum, and microscopic section showed a rather small sarcoma of the stomach (slide) The sarcoma was obviously cellular and contained a number of vascular spaces that might tempt one to place this tumor in some special classification Ewing, however, holds that vascular spaces of this type do not warrant bizarre classification of the tumor The slide also demonstrates over the tumor the site of an ulcer which had healed under medical management

The final patient to be reported was a man, age 70, who had developed symptoms referable to the stomach nine months prior to registration at the Clinic Ultimately, a diagnosis of polyposis of the stomach was established and subtotal gastrectomy was performed (slides) It is unusual for polypoid proliferation to so closely follow the lines of the mucosal rugae that there are no true isolated polypoid tumors, but rather polypoid hyperplasia of the entire mucosa The microscopic section shows the rather curious cystic hyperplasia of mucosal glands which occurs in polyposis of the stomach

DR CHARLES C GREEN, Houston, Texas I should like to comment on Col Griswold's paper Two years ago I heard an excellent presentation on this subject read before the Texas Surgical Society by Major Coleman, one of our guests today, and he showed a wonderful motion picture of his surgical technic of the transpleural approach

to lesions of the upper abdomen I am glad to hear Col Griswold recommend the resection of the tenth rib I have never done this but I believe it will give a more flexible opening and an easy approach I think it is one of the greatest advances in upper abdominal surgery

DR FRANK H LAFFY, Boston, Mass From my point of view it is safer to make the exploration to determine operability in many lesions situated very low in the esophagus through the abdomen rather than through the pleural cavity A small incision through the abdomen permits the patient to get up and around in a day or two and often more readily settles the question of operability than does chest exploration If one chooses to operate in two stages for lesions low in the esophagus, the stomach can, by the abdominal route, then be devascularized, and the omentum can be taken off The omentum so often contains metastases in these cases that omentectomy is worth doing In addition, the spleen can be removed when the omentum is taken off abdominally, which makes for easier handling, wider removal, and, thus, increased radicalness when the second stage is done through the chest Furthermore, removal of some of the high gastric lesions can be done more safely from below by a total gastrectomy, than from above, as transthoracic resection We have now done more than 90 total gastrectomies, and the mortality, certainly in the last 25 is down around 10 per cent

Some time ago we suggested that in all cases of gastric cancer, the stomach be irrigated preoperatively with 0.7 per cent hydrochloric acid, because by this means the bacterial count in the gastric contents can be almost entirely eliminated prior to operation

With regard to Doctor Rienhoff's paper on peptic ulcer, I have just sent an editorial to one of the surgical journals on this subject in which I stated that the mortality of subtotal gastrectomy for ulcer today has resolved itself, in our hands, almost solely to the proximity of the ulcer to the common duct Peritonitis as a mortality factor together with pneumonia, has been practically eliminated

We feel very strongly that as we have increased our experience with subtotal gastrectomy in patients with duodenal ulcer, we have removed more and more ulcers and the results have been better, we feel very strongly that the Finsterer operation by exclusion is a bad operation In it we have seen more recurrent gastrojejunal ulcers in the gastric stump than have occurred following subtotal gastrectomy in which all of the pylorus and prepyloric region is removed We feel strongly, likewise, that the results have been better in subtotal gastrectomy when we have taken out that portion of the duodenum containing the ulcer

I would like to submit a plan, which I have also just sent for publication, which makes the removal of these ulcers easier, that is, a T-tube is inserted into the common duct, the sphincter of Oddi is dilated, and the tube is passed through the duct into the duodenum It is a great comfort to know where the sphincter of Oddi is If the tube protrudes through it, you can put your finger on it, know the level at which it enters, and you know how much duodenal stump there is left You can also be sure of the location of the duct behind the duodenum as it passes through the indurated bed of the pancreas

As to the amount of stomach to be removed, everyone has to settle that for himself I do not think that is as important as removal of the ulcer We have seen enough cases in which the ulcer has been left behind in which a jejunal ulcer has occurred in the stump and in which secondary removal of the ulcer has resulted in healing of the gastrojejunal ulcer in the stump of the stomach, that we are convinced that leaving ulcers is undesirable

We realize that there are occasional ulcers which are so indurated and so scarred that no plan exists whereby they can be removed safely, and we realize that in these cases a two-stage operation, such as the Finsterer resection by exclusion or a high gastroenterostomy, with a deliberate plan for a second-stage removal of the ulcer when it has healed, has a real place

COLONEL I MINIS GAGI, Atlanta, Ga The edited transcript was not received in time for publication If it is received before the "Transactions of the Southern Surgical Association" is published, it will appear therein

DR DIRK HART, Durham, N C This discussion will be limited to the question of treatment of severe hemorrhages from ulcers. There is a fairly widespread opinion that operation in the presence of a low hemoglobin due to repeated severe hemorrhage is followed by an almost prohibitively high mortality. Our experience has been that we can delay operation, use repeated transfusions, and have the hemorrhages stop in most cases, with a very low mortality in the nonoperative cases. As a result of this method of treatment, however, patients coming to operation have been the poorest surgical risks, but by the use of large quantities of blood (1500 to 4000 cc) immediately before and during operation the mortality in the operative cases has also been kept low.

Of a total of 1318 ulcer patients admitted to the hospital, 275 (21 per cent) have come in with bleeding at time of admission, 79 had an hemoglobin below 50 per cent. Of this latter group 66 were treated by non-operative methods with one death, a mortality of 1.5 per cent. Thirteen continued to bleed and were operated upon, with one death, giving a mortality of 7.7 per cent in the operative group. The one death following operation was in a patient with an ulcer low down (at or below the anipulla of Vater) in the duodenum, making resection impossible. An exclusion operation was performed, bleeding continued from the ulcer, and death was due to hemorrhage. The mortality for the entire group of patients whose hemoglobin was below 50 per cent was 2.5 per cent.

From this experience we feel that patients with a bleeding ulcer should be treated first by nonoperative measures. In the small group where such treatment fails, operation can be performed with relative safety if large quantities of blood are given before and during operation. With such a regimen the total mortality has been lower than would have been likely had a high percentage been treated surgically soon after admission.

CORONEL R. A. GRISWOLD, M C, Washington, D C (closing) With regard to Doctor Lahey's remarks, we have not irrigated the stomach in cases where there was no stasis, however, we have administered dilute hydrochloric acid either by mouth or tube in those cases with achlorhydria. I cannot agree with Doctor Lahey on the danger of the thoracic approach. The thoracic surgeons have shown us that the chest can be entered with the same impunity as the abdomen, if proper attention is paid to respiratory physiology. In tumors of the upper stomach and lower esophagus, the operation is certainly easier with the lesion directly in the middle of the field rather than up under the dome of the diaphragm. If necessary, total gastrectomy may be carried out by the thoracic approach as well as by abdominal route.

DR WILLIAM F. RILNHOF, JR, Baltimore, Md (closing) I have enjoyed the discussions of Doctors Horsley, Sanders and Lahey very much indeed. It is my opinion that the antecolic gastrojejunostomy or anterior Polya type of anastomosis is to be preferred rather than the Billroth-I as suggested by Doctor Horsley, the reasons being (1) shunting the gastric contents away from the duodenum insures more prompt healing of an ulcer in this region, and (2) neutralization is more complete when jejunal contents are constantly irrigating the remaining gastric pouch. I agree with Doctor Sanders that there is a definite group of cases, *et al*, older individuals with a scarred and stenotic pylorus, in which a simple posterior gastro-enterostomy is the operation of choice.

Doctor Lahey's point about performing a total gastrectomy abdominally instead of transthoracically is interesting. Doctor Longmire, our resident surgeon, has had a most unusual series of cases with carcinoma of the stomach in which he has performed a total gastrectomy intra-abdominally without a death. Except in instances in which the lower end of the esophagus is involved, the operation may be performed, as Doctor Lahey suggests, with fewer hazards if confined to the abdomen.

I hope Doctor Lahey will not mind if I differ with him on one point, that is the necessity of dissecting out all ulcers of the duodenum. I believe this is unnecessary in the great majority of patients and that the ulcer will heal if isolated from the flow of gastric contents and put at rest. I do not believe there is any connection between the presence of an ulcer in the inverted duodenal stump and the occurrence of a postoperative peptic ulcer of the jejunum.

DR SAMUEL F MARSHALL, Boston, Mass (closing) One must emphasize, as Doctor Rienhoff has done in his presentation, that, after all, the patients who finally come to the surgeon for treatment represent the failures under medical management, or the patients with serious complicated ulcers who cannot be relieved of their symptoms without some form of surgical procedure. I am sure that the ulcer recurrence rate can be greatly reduced by an adequate resection of the stomach. In our own experience, approximately only 7 per cent of patients with duodenal ulcers required operation. During a period of seven years we have done resection in 367 consecutive cases and of this group, 62 were done for jejunal or recurrent ulcer, with a mortality of 2.2 per cent for the entire group. Our rate of recurrence of ulcer in this group is probably less than 3 per cent.

With regard to gastrojejunocolic fistula, the question has been raised relative to removal of so much colon, whether it is necessary to carry out such a radical procedure. We know that in some cases with small fistulae, with only moderate amount of inflammatory reaction about the fistulous tract, one can excise the fistula and restore normal continuity of bowel, but it is with this type of operation that the mortality has been so high. If resection of the colon is necessary it is much safer to remove the right colon and transverse colon to a point beyond the fistula than it is to do a segmental resection and to attempt a primary colon anastomosis. Our own experience has demonstrated that the mortality can be reduced by the procedure presented here today, that the involved colon and jejunum can be more safely removed in this manner, and that this removal makes resection of the stomach much easier.

FULL-THICKNESS SKIN GRAFTS FROM THE NECK FOR FUNCTION AND COLOR IN EYELID AND FACE REPAIRS

LT COL JAMES BARRETT BROWN, M C

ST LOUIS, MO

AND

MAJOR BRADFORD CANNON, M C

BOSTON, MASS

FULL-THICKNESS GRAFTS from the neck and the clavicular region have been found to give superior results in the repair of facial defects. The amount of skin available is limited, but there is enough for eyelids, the nose, and about the mouth.

Two main advantages are improved function and color. The graft was first used on the lid, and many full replacements of the lid skin hardly can be distinguished at only two or three feet distance. The color is nearly always close to that of the normal face and is due to the good color of the neck skin, plus the good function that is possible, and to the actual extra thickness that these grafts have over the usual thick-split or full-thickness graft. None of these grafts so far have had to have pigment injection for color matching, whereas, dead whiteness or darkness of other grafts often leaves much to be desired. There is natural redness in these grafts not found in other skin and this redness is the reason for the match with the surrounding skin. (On a burned face that has healed to a dead white, these grafts give a noticeable contrast, although they are the closest to normal.)

The second advantage is softness and, therefore, function. This function, of course, is of underlying muscles, but these grafts heal in so soft and have such thickness that the best kinesis of grafted areas can develop. This property again is best expressed in eyelid repairs, where hard, board-like scars of gasoline and phosphorus burns have to be literally dug out of the lids and across from one eye to the other over the nose. When these areas are covered with the neck grafts, there is often a dramatic relief of scar fixation and return of softness and function.

The good function is due to the thickness and softness, and possibly because of the character of the skin which, in its natural habitat, overlies a platysmal muscle. This point has not been proven so far, but the result of an eyelid's being soft, of normal color, giving normal function, healed in, with practically no edge scar, in two to three weeks after grafting, brings up the platysmal idea.

Late function is excellent as there is minimal contraction of the graft bed when these grafts are used.

* Read before the Fifty-sixth Annual Session of the Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

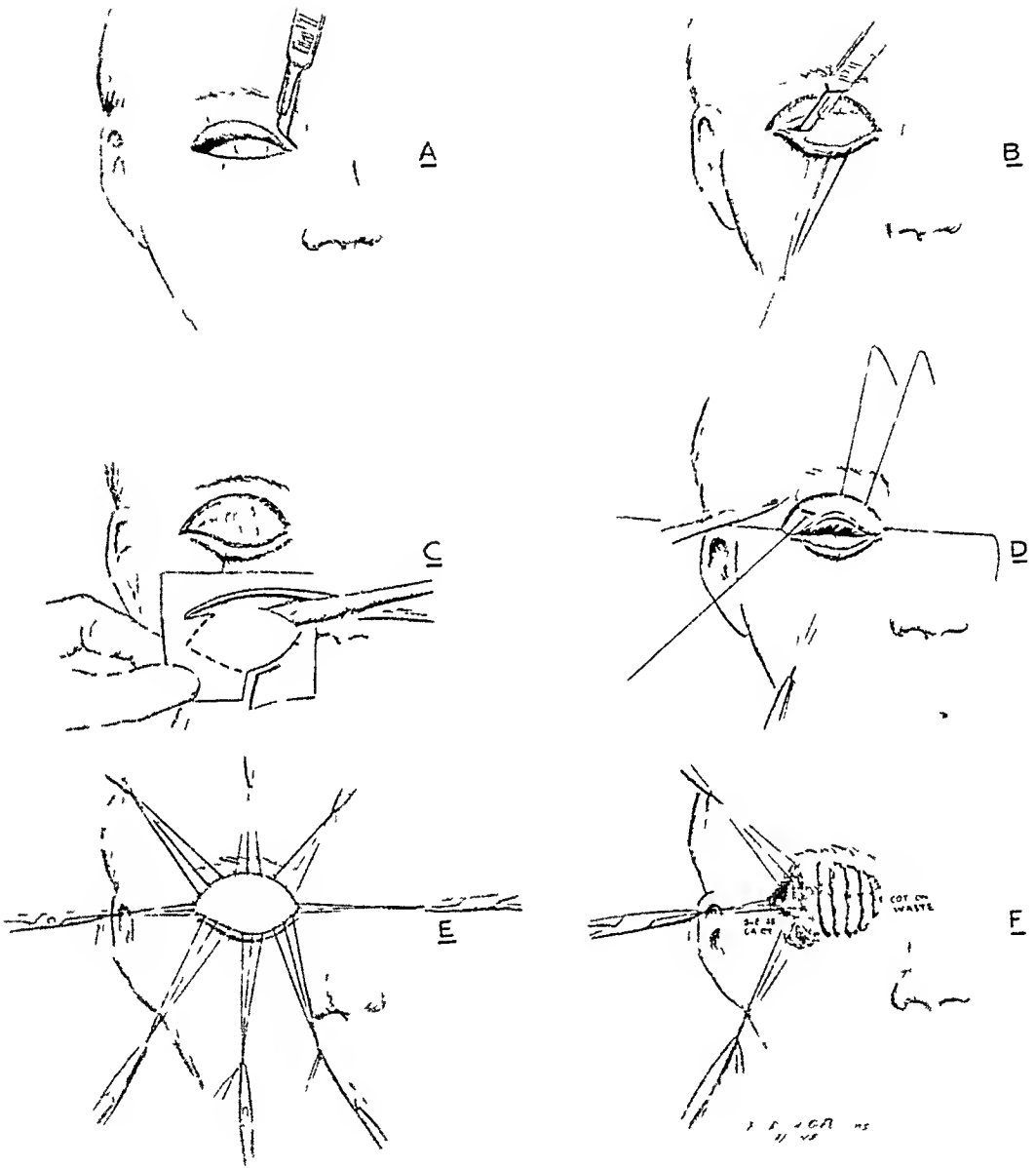


FIG 4—Contracted area opened surface and deep scar removed as necessary, to allow a little more than normal expanse. Where pressure alone can not be relied on—as on the lids—the fixation is obtained and the proper opening of the area and the proper stretch of the graft obtained by the long sutures being tied over cotton mechanics waste carefully packed into place, after covering the area with fine mesh grease gauze.

This graft is usually superior in color and function, and fairly normal color match with graft from other preferred areas, such as the mastoid and inguinal regions.

The main areas for use are on the lids, in the canthal regions, about the

FIG 1a 1b—Restoration of lid skin and function, and fairly normal color match with graft from neck. One operation.

FIG 2a 2b—Restoration of skin of both lids, and function and color with neck graft. Older graft around inner which was taken from a distant area shows variation in color. One operation for each lid.

FIG 3—Repair of contracture of lower lip with graft from neck, color match and function about normal. One operation. Color can be compared with grafts on upper lip, which were not from neck. Color injection of the upper lip has been done later by Miss Gertrude Hance, in consultation with Dr. L. T. Byars.



FIG 1A



FIG 1B



FIG 2A



FIG 2B



FIG 3

ala, over the nose and about the lips and angles of the mouth. As a rule, flap repairs are considered for gunshot wounds, whereas, grafts usually suffice for burns. However, about the lids, if a bed at all suitable can be obtained by dissection of the scars, these full-thickness grafts are used in preference to flaps and, it is thought, with better results.

Donor sites can be closed, left open to granulate, or grafted. They may make troublesome scars for a while, but no permanent severe trouble has been

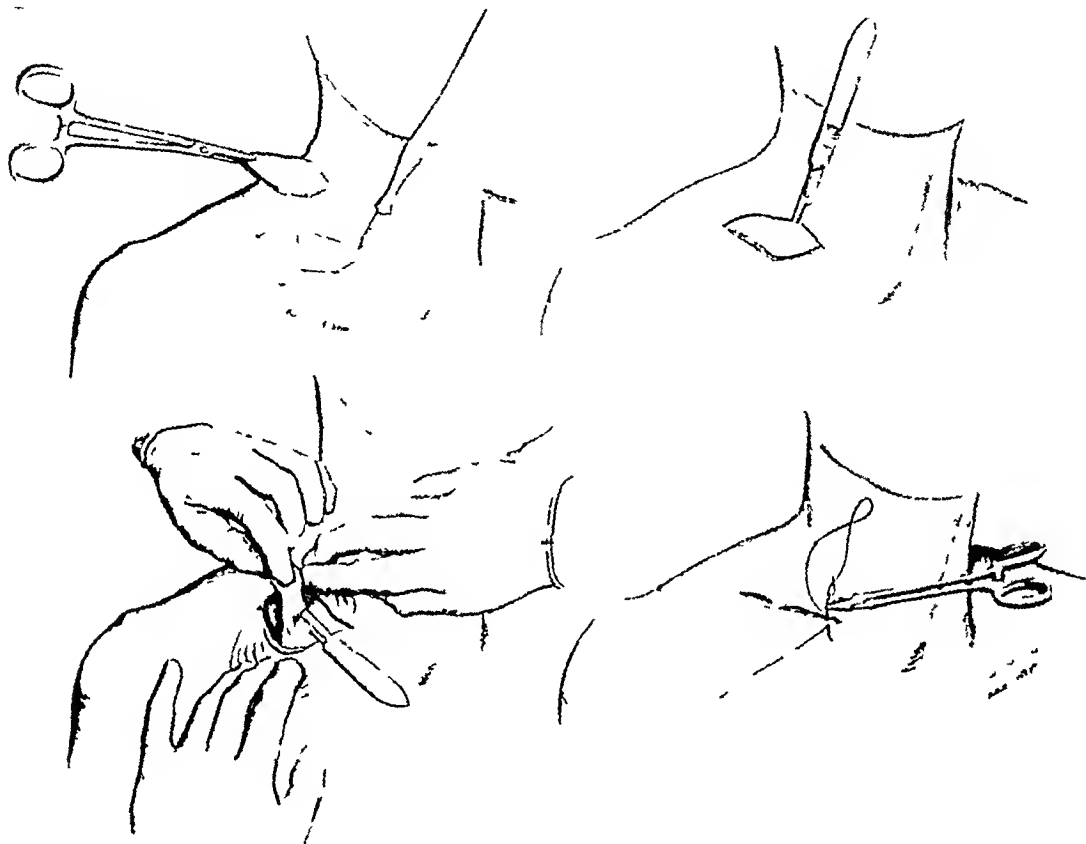


FIG. 5—Celluloid or phiofilm pattern marked on neck, tension produced by assistants for ease of removal, fingers hold graft to avoid crushing. Wound closed.

seen. Large scars would be objectionable in women, but this does not preclude the use of small grafts.

TECHNIC OF PROCEDURE

The scarred or deformed area is dissected free and the edges are moved back to their normal position carefully, so that they are not undermined or too irregular and so that an accurate fit (or set in) of the graft can be done. With this excellent graft available, careful dissection can be done and repositioning of parts fully carried out, with the thought of accurately filling the defect and counting on only the slightest contracture of the graft bed. The pattern of the defect, in phiofilm or celluloid (roentgenogram film), is marked out usually just above the inner third of the clavicle either with methylene blue or directly with the knife. The graft is removed in the usual manner, with good firm stretching by assistants to produce a "drumhead" to work on

After an edge is freed, fingers are used to hold the graft instead of forceps or hooks and the dissection is completed carefully at the proper full-thickness depth so that no trimming of the under surface of the graft has to be done later. These grafts appear so thick that their growth might seem questionable, but growth of them has been as good as of split grafts, and there has been none of the spotty necrosis sometimes seen in full-thickness grafts.

Donor sites are usually closed, or are partly closed and partly left open, or covered with a split graft.



FIG 6—Resurfacing of right upper lip with graft from neck after correction of deformity and reconstruction of nostril. Color match and function about normal. Two operations.



FIG 7—Complete fixation of tongue in scar, released by dissection, the resulting raw surface covered with graft from neck in endeavor to get good soft tissue to allow function. Good movement has been permitted from one operation. Lined flap has been delayed on neck for final repair.

Application of Grafts—These grafts are set in accurately with interrupted sutures of light silk, every two to four millimeters around the borders. The ends of the sutures are left three to four inches long for subsequent fixation of a waste form, and each two sutures are clamped with a mosquito clamp. No holes are cut in the graft. The graft is covered with fine mesh grease-gauze and a wad or form of white cotton, mechanics waste is packed carefully over this, to assure firm coverage of the entire graft.

Appropriate opposite sutures in pairs are selected for the first anchorage

and as the assistant firmly compresses the waste with his fingers or instrument these opposing sutures are firmly tied over the waste. The remaining sutures are tied over the waste in pairs. The eye is protected with a suture closing the lids if necessary, and usually a larger over-all waste pressure dressing is applied, with a gauze roll going around the head, to obtain counter pressure posteriorly. This fixes the whole area and is usually more comfortable than just the small waste form without further fixation.

Dressings are done on the 3rd to 6th day, and subsequent ones are repeated as necessary, usually having them off about the 10th day.

Suturing these grafts in place is essential if a full edge-to-edge take is desired. Contracted areas, such as on the lid, are dissected and then are pulled outward with the sutures over the waste to establish the complete area of opening and the fixation at the same time. A gluing method of fixation is not applicable by itself, though it also may be used if its added fixation is thought to be of benefit.

Because these grafts have been widely used, some chances of infection have naturally been taken about the mouth and nose, but there have been no full-thickness losses. A few have desquamated some epithelium, and have been brown and then red for a fairly long period, but this has finally cleared up, with some residual redness and a slight glaziness.

The graft has been used successfully to free a totally restricted tongue, and its use on fingers and on the penis is contemplated.

This may be recognized as a standard full-thickness graft procedure, but is recorded because of the evident worth in function and in color. The slight extra work and extra care of the donor site over the usual split graft or full-thickness graft is thought to be indicated in many repairs.

This work has been done in association with Captain Carl Lischer, Captain Parke Scarborough, Lt Bowdoin Davis, Lt Andrew Moore and Lt Col James N Greear, Jr, and his associates on the Eye Service.

TATTOOING OF FREE SKIN GRAFTS AND PEDICLE FLAPS^{*}

LOUIS T BYARS, M D

St Louis, Mo

FROM THE DEPARTMENT OF SURGERY WASHINGTON UNIVERSITY SCHOOL OF MEDICINE ST LOUIS MO

SKIN COLOR is partially due to the presence of certain pigments of the skin, as in the Negro or the dark complexioned individual. Another factor producing color variations in various areas of the body is the type of blood flow through the skin. For example, a small scratch on the face may bleed annoyingly for several minutes, whereas a similar cut elsewhere on the body may bleed but a drop or two. It is chiefly this factor of capillary flow which gives the red tone to the skin of the face, ears or neck. Of necessity, free skin grafts or pedicle flaps are often applied to the face. When free skin grafts are taken from the postauricular region or from above the clavicle and applied to the face they usually match the skin well in color. Pedicle flaps of forehead tissue also match the face well in color but necessitate the use of skin from elsewhere to cover the defect of the donor site. Skin taken from other parts of the body and applied to the face may be whiter or darker than face skin, but the chief factor in the color contrast is the absence of the red tone (Fig 1).

Heretofore, after function and contour had been restored by surgery, the patient often had to resort to the use of cosmetics for a reasonably good appearance. This has been for the most part unsatisfactory, especially with men. During the past eight years, the cautious but increased use of pigment injected permanently into the derma has proven a safe and satisfactory adjunct to surgery to produce a better cosmetic result¹.

Tattooing is the practice of depositing permanent pigments within the skin and has been employed for thousands of years, either for decorative or religious purposes or to produce marks of identification. It probably has been used in an attempt to hide blemishes, and we have seen a number of patients who have crudely tattooed themselves in an effort to eliminate or camouflage bald areas in the brows or scalp. There is very little in medical literature to indicate this use of the procedure. The tattooing of white corneal scars overlying the dark pupil of the eye has been done with considerable improvement in the appearance of the eye. It is obvious that the pigments employed must be nonpoisonous, nonirritating to tissues, extremely insoluble and inert to body metabolism. The pigments which we have employed have been provided by those firms supplying tattooing equipment to professional practitioners. Chemically, there is probably considerable variation in their content as there is in their shade. Black is carbon, white is barium sulphate. For the most part, the yellows, browns and reds are earthy metallic oxides, the color being

^{*} Read before the Fifty-sixth Annual Session of the Southern Surgical Association, December 5-7, 1944, Hot Springs, Va

controlled by the amounts of hematite and limonite present. Clay or chalk is sometimes contained. Cinnabar, mercuric sulphide, is one of the red pigments sometimes used. Umber, a brown ocher, contains some manganese.

*Technic**—The procedure is carried out in as near an aseptic manner as possible. The area is prepared with soap and water and alcohol, the pigments are autoclaved and the instruments sterilized. The skin must be free from infection. The procedure is somewhat painful except when used on a skin graft or flap which has not yet regained its sensation. In hospitalized patients, analgesia may be obtained with the barbiturates. Otherwise a

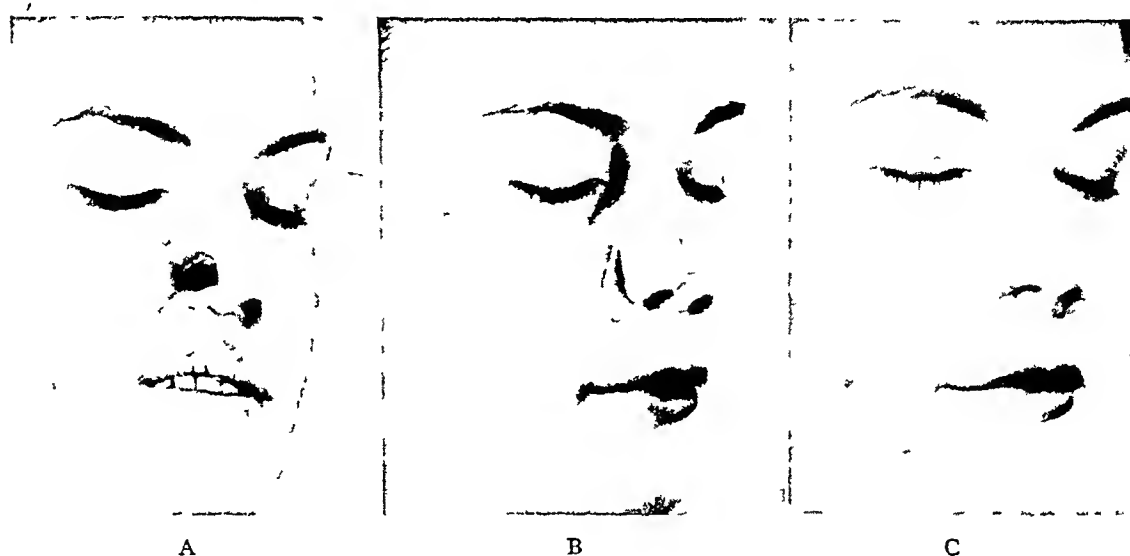


FIG. 1.—A Defect resulting from destruction of a malignant lesion involving the ala of the nose and adjacent cheek.
B Repair partially completed with two flaps, one to piece out the cheek and the other to form the ala. The cheek flap has been pigmented by color injection and the contrast is shown between this and the nose flap which still has its original color. Transplanted tissue was from the arm.
C Final result and after pigmentation of both cheek and nose flap to match adjacent tissues.

novocaine block of the area is more satisfactory than infiltration anesthesia. The dry pigments are mixed thoroughly on a clean glass slab and moistened with normal saline until about the consistency of thick cream. For matching a graft to the face skin, one starts with small amounts of red, yellow and white. The correct mixture will be a shade darker than the skin. Spreading a thin coat of the trial mixture over the contrasting area helps in obtaining a match. Often after the red, yellow and white are blended, a small drop of black is added. The mixture must be blended in different proportions in almost every case.

Professional tattooers use an electrical vibrator with multiple needles to carry the pigment into the skin. This is a rapid method and it is essential in doing large areas. Unless one has developed self-assurance, it is perhaps better to proceed more slowly, using multiple needle points soldered to a handle to prick the pigment into the derma by hand. The pigment is picked up on the points and the needles inserted obliquely into the depths of the

* Pigment injection was undertaken on the illustrated cases by Miss Gertrude Hance, 400 Metropolitan Building, St. Louis, Mo.

skin. The needle pricks must be very close together, although with time there is dispersion of the pigment, which gives a more uniform appearance and relieves the splotchy early appearance. The excess pigment is constantly wiped from the surface so that the evenness of the injection may be observed. There is a period of fairly severe inflammation, lasting a week or ten days, following which there is desquamation of the surface. The color gradually diffuses and pales somewhat. Patchy areas may appear. A second treatment is often needed, at which time color discrepancies can be corrected and patchy areas blended. It is better to err on the side of under- rather than over-pigmentation.



FIG. 2.—Upper picture shows thin atrophic scar resulting from irradiation of an angioma. The middle picture shows the lesion replaced with a pedicle flap from the arm. The color contrast between the transplanted tissue and the forehead is definite. The lower picture shows color matching of the transplant to adjacent tissue by pigment injection.

approaches normal. For this reason it is better to wait until a graft has achieved its greatest degree of relaxation and flexibility. Such a skin graft may be dead-white, yellowish, or brown. The white graft is of course most ideal but by taking into consideration the color of the graft when blending pigments it is possible to improve greatly the color match of even the less ideal areas (Fig. 3).

Selection of Cases—In general, the uses of this procedure are (1) to match contrasting areas, such as skin grafts, to the surrounding facial skin (Fig. 3), (2) to simulate missing vermilion of the lip, (3) to blend in rather patchy scarred areas to give a more uniform appearance, and (4) to camouflage bald areas within the eyebrows.

Hard scarring interferes with the process of insertion and spread of the pigment, soft scars are amenable to injection.

We have had little experience with its use in the Negro. In one such case where irregular areas of depigmented scar were present on the nose and forehead as the result of a burn, Lt. Col. James Barrett Brown employed the procedure with some success at Valley Forge General Hospital.

Skin Grafts—New skin grafts are thick and leathery. As they get older the quality of the skin more closely

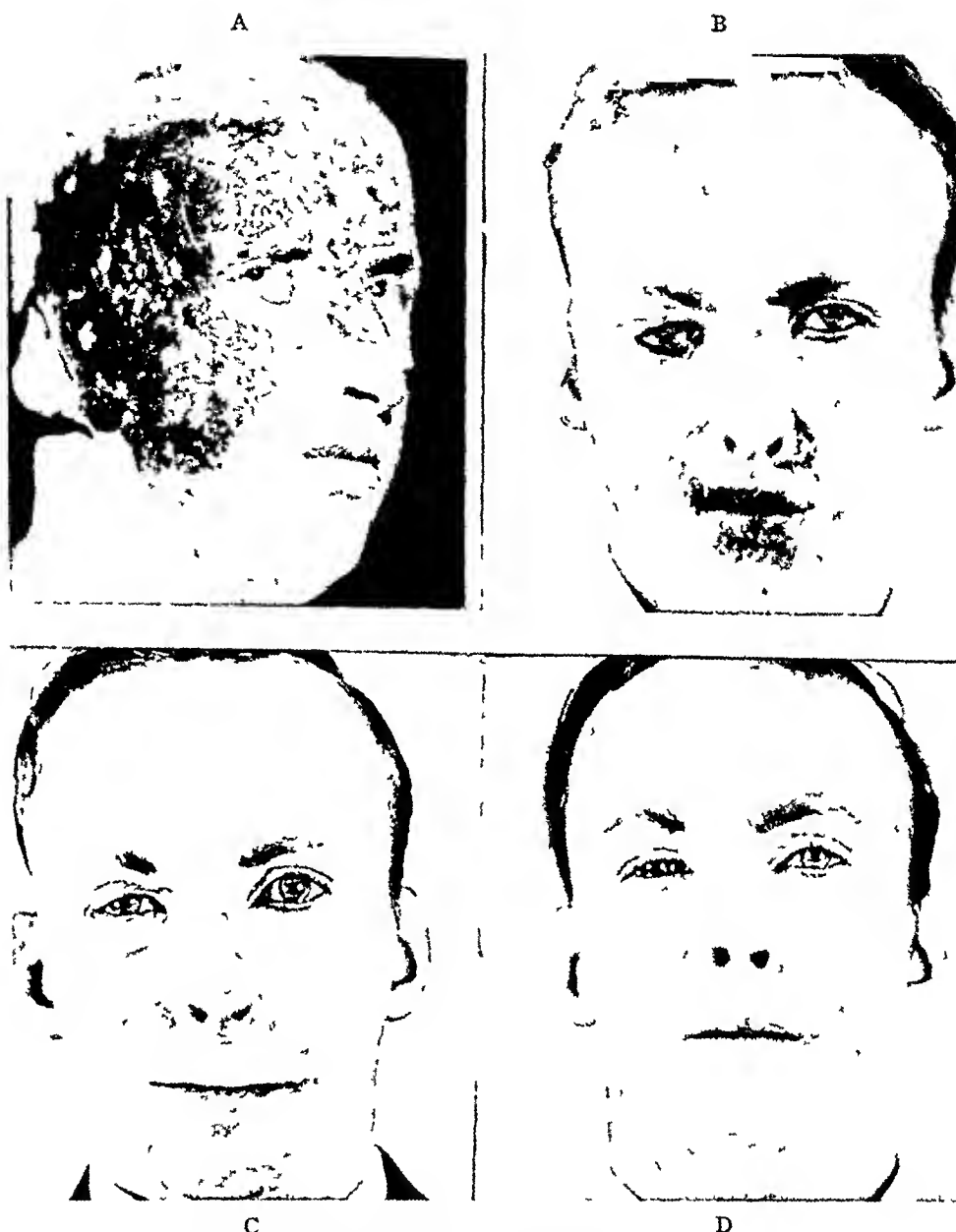


FIG. 3—A Original condition six weeks after burn
 B Healing obtained at first operation by applying split graft to the granulating wound. Considerable keloiding has developed in the areas which healed spontaneously and there is a marked ectropion of the lower eyelid on the right
 C Repair as far as contour and function has been completed. Lower eyelid is in good position. The heavy scarring about the face has been removed and replaced with free full thickness skin grafts. These grafts are very white and quite noticeable
 D Skin grafts have been matched to adjacent tissue by pigment injection. Note the vermilion of the upper lip which has been emphasized by the same process. Partially missing right eyebrow has been camouflaged in the same manner

Skin Flaps—The texture of the pedicle flap is often better than that of the free skin graft and does not require as long a period to become soft and pliable. Usually, the color of the pedicle flap remains much as it was on the donor site. There does not seem to be the tendency to discoloration from condensation of pigment as occurs with the thinner free grafts. The flap is more commonly used in the reconstruction of features, such as the nose, lip, or full-thickness of the cheek (Figs 1 and 2). Oftentimes the total area of the face covered by flap is not nearly as great as with the free skin graft which has been used to correct a widespread burn.

Vermilion of the Lip—Regardless of the perfection of contour of the reconstructed lip, the appearance is artificial without a vermilion. The use of lip-stick is not satisfactory because lip-stick does not produce the normal, unretouched vermilion, and with men its use is obviously undesirable. When lip-stick is smeared, the underlying absence of the vermilion is doubly noticeable. The vermilion is occasionally destroyed fully or in part by chemical or fire burns, and the simulation of the normal vermilion in either situation aids greatly in producing a normal-looking result (Fig 3).

Bald Areas—Bald areas in the eyebrow may be well camouflaged (Fig 3). An attempt to simulate an entire missing eyebrow gives the same effect as the use of an eyebrow pencil. Occasionally small bald areas within the scalp may be made less noticeable. One should be cautious in attempting to stipple a bald area on the bearded portion of the face. This is likely to cause a dirty appearance, which would be unsatisfactory.

SUMMARY

Intradermal pigment injection has been undertaken in over 60 cases for the purpose of matching skin grafts and flaps to adjacent facial tissue. There have been no complications. In each case improvement was gained. The degree of improvement varies with the type of case and skill of injection. This procedure has been regarded by the patients as being well worth while.

REFERENCE

- ¹ Hance, Brown, Byars, McDowell. Surg., Gynec. and Obstet., 79, 624, 1944.

DISCUSSION—DR JOHN STAIGE DAVIS, Baltimore, Md. I was very much interested in both these papers. What Colonel Brown has shown us is the highest type of military plastic surgery. It has been my privilege to be at Valley Forge Hospital on more than one occasion and I have seen some of the extraordinary plastic surgery being done there. It is an eye-opener, nobody who has not seen what is going on can realize the magnificent work being done in the hospital. I was greatly impressed with the morale of the patients in the plastic wards, it was unbelievable. These men, with terrific deformities of all types, are cheerful and hopeful, it is marvelous to see how they are handled, and I take my hat off to Colonel Brown, and his associates, for the way the morale of these men is kept up.

The procedure described in Doctor Byars' paper is unquestionably a very useful one. I have, so far, not had anyone who was capable of doing these injections properly, but I hope to have someone trained to take care of the glaring white defects and the defects in eyebrows and lips. His method, I think, will bring about a wider use as the technique becomes known.

TANTALUM CRANIOPLASTY FOR WAR WOUNDS OF THE SKULL*

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AND

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THE REPAIR of skull defects resulting from war wounds of the head has become a major task of the rehabilitation neurosurgeon. During the past year head injuries comprised 59 per cent of our total casualties and approximately one-fifth of these were open head wounds. The care of such injuries is divided by the very nature of the lesion among several echelons of medical support. In the first place, it has been estimated that 50-60 per cent of the men never seen alive again after entering a decisive engagement have fatal wounds of the head, although they may exhibit other potentially fatal injuries as well. The mortality among those that survive varies between 15 per cent¹ to 14 per cent² to 22 per cent³. The preservation of life and the prevention of infection by débridement and primary closure are the functions of the evacuation hospital or the special surgical unit, the treatment of infection and the guidance of the late stages of convalescence are the responsibilities of the base or numbered overseas general hospitals.

As we have pointed out recently,⁴ when the patient with a healed head injury returns to the Zone of the Interior he presents one of two problems and frequently both. The first comprises an evaluation of the existing neurologic defect, carried out by neurologic and psychiatric surveys supplemented by electro-encephalography and pneumo-encephalography. Such an evaluation is a pertinent factor in determining disposition to duty or some other status. The second problem is that of repairing skull defects in otherwise fit individuals for return to duty or in patients whose skull defect represents merely a part of a disabling cerebral injury. The repair of such skull defects in Army personnel, caused by gunshot wounds and by operative relief of traumatic intracranial hematomas and as a sequel of cerebral tumor or infection has been carried out in 79 patients at the Walter Reed General Hospital for the most part during the past 11 months. Half of these patients have thus far been returned to some type of duty. An incomplete estimate of the magnitude of this problem may be derived from the statement that the Walter Reed General Hospital is but one of 19 neurosurgical centers in the Zone of the Interior.

Before the repair of a skull defect is accomplished in any one patient an evaluation, not only of the existing neurologic defect, but also of the potential epileptogenic activity of the concomitant cerebral scar is attempted. With the time interval between initial injury and our observation of these cases steadily lengthening, it has become apparent that the posttraumatic

* Read before the Fifty-sixth Annual Session of the Southern Surgical Association, December 5-7 1944, Hot Springs, Va.

† This report was prepared while Lt Col Spurling was on overseas duty.

convulsive state will be an important disabling sequel of penetrating injuries of the brain, as it has been in the past. Studies to be published shortly⁵ show that in a series of 76 penetrating injuries of the brain observed over a time period of approximately one year or less, 15 have developed convulsions within four months of the injury and that a further 15, a total of 40

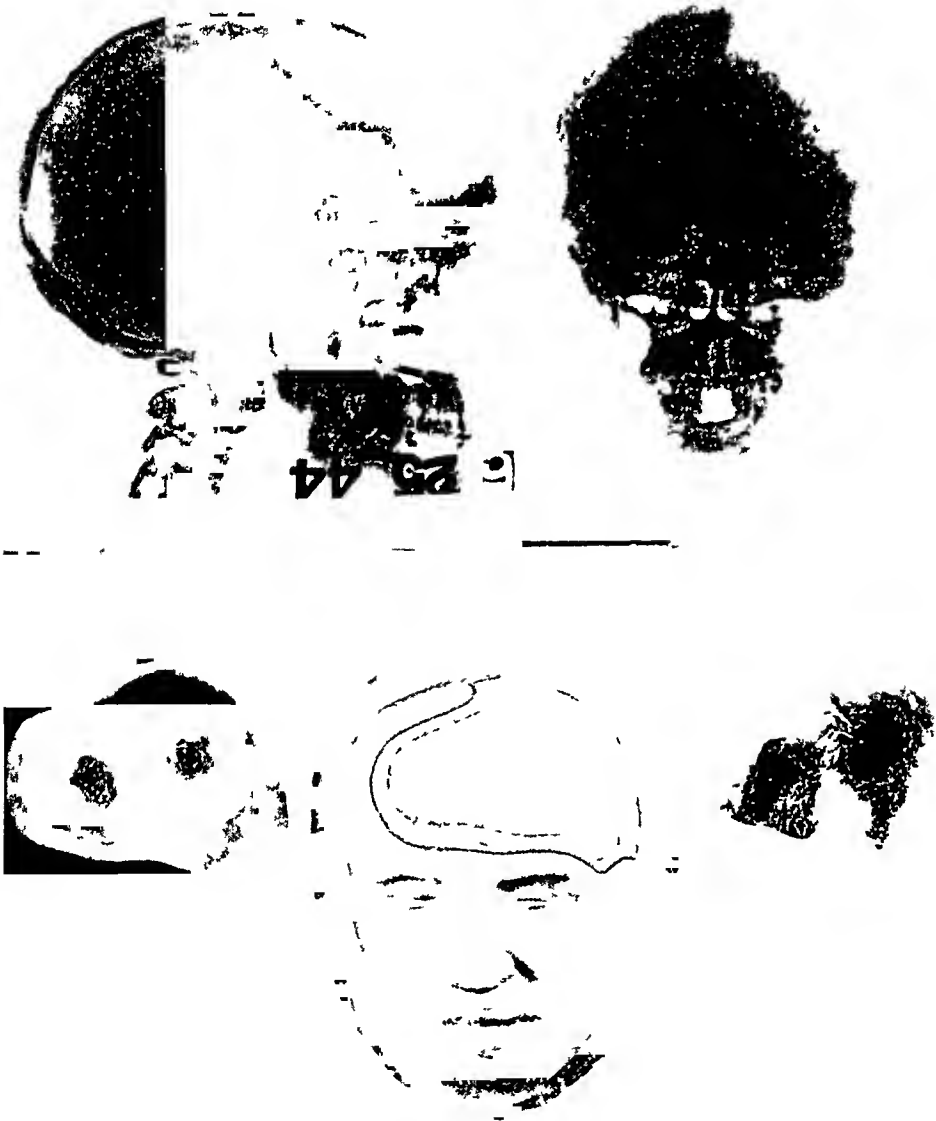


FIG 1—Extensive bifrontal defect following a mine explosion. The dental stone impression of the defect, the wax restoration and the completed tantalum plate are illustrated.

per cent, now exhibit electrical cortical activity highly suggestive of an epileptogenic focus. It may be noted in passing that these patients have shown a highly favorable if early response to the conservative regimens of treatment developed during recent years.

INDICATIONS FOR CRANIOPLASTY

The indications for the repair of a skull defect have been established by

the observations made upon many patients by numerous surgeons and have been stated succinctly in the classical paper upon this subject by Grant and Norcross⁶ Such indications include

(1) Headache and other symptoms of the syndrome of the trephined, including vertigo, local tenderness, fear of injury and a subjective feeling of insecurity, easy fatigability, mental depression and intolerance to vibration

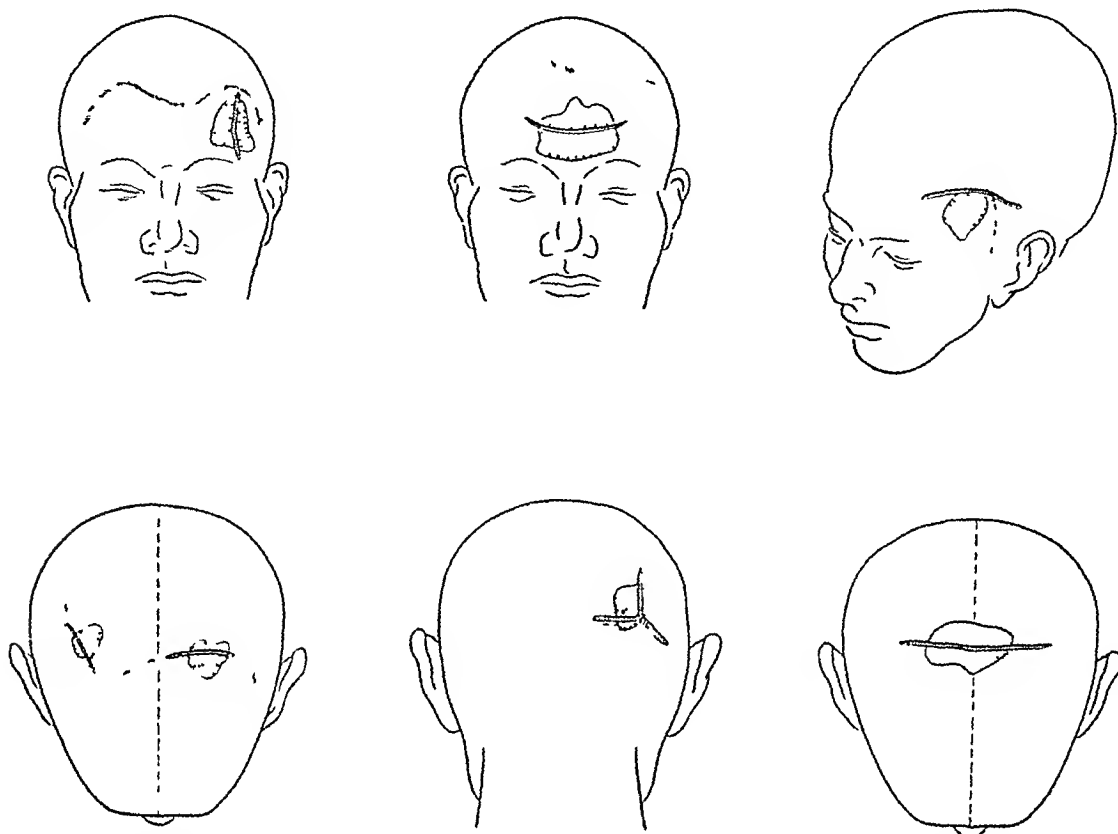


FIG 2—Various scalp scars following debridement of the initial injury. The proposed scalp incisions for cranioplasty are indicated with broken lines

- (2) Undue pulsation of the underlying brain
- (3) Exposure to trauma of the underlying brain
- (4) Cases with deforming and repulsive defects, and
- (5) The assumed relief of an associated convulsive state

To these more or less cogent reasons, may be added certain military regulations governing the handling and disposition of such patients when they are treated under service conditions. Under AR 40-105, par 23 e, an applicant for a commission in the Army of the United States may be rejected for "depressed fracture or loss of bony substance of the skull." Under MR 1-9, an individual fails to meet minimum requirements for induction into the Army if under par 40 a, he possesses "deformities of the skull in the nature of depressions, exostoses, *etc* , of a degree which would prevent the individual from wearing military headgear." The profile supplement to MR 1-9 places patients with skull defects of this character in a permanent restricted duty status, and in order to gain a more advanced duty status, cranioplasty is indicated.

Thus, in the practice of military neurosurgery, it is imperative to repair all skull defects over three centimeters in diameter if a return to duty status is desired. That this is advisable in the rugged existence of Army service is validated in part at least by three isolated instances that have come under our personal observation.

Case 1—P S S, Reg No 210122, age 23, was operated upon in the Walter Reed General Hospital on July 31, 1942, for the relief of an acute subdural hematoma in the left temporal region, the result of a baseball injury sustained on July 17. A four-centimeter skull defect in the left temporal region and a two-centimeter defect in the left temporal region were caused by the operative procedure. His convalescence was without incident and he was returned to duty. On March 6, 1944, he took part in a grudge fight with regulation boxing gloves. He received a series of blows on the



FIG 3—Case 1 Bifrontal skull defect caused by fragment of aerial torpedo

head and 48 hours later, bilateral subdural hematomas were drained at this hospital through the preexisting skull defects.

Case 2—M F S, Reg No 195005, Walter Reed General Hospital, age 27, was struck in the left frontal region by a bayonet on January 9, 1942. The resulting compound comminuted skull fracture and cerebral laceration were debrided after resection of a 3-4 centimeter bony defect. After return to duty, he developed severe head pain, localized at the point of injury, from the pressure of a steel helmet. His symptoms were relieved by tantalum cranioplasty on July 17, 1943, with subsequent return to active duty.

Case 3—Ashford General Hospital W W, age 24, a fighter pilot, assayed a return to duty with a small 3.5 centimeter defect in the right occipital region. Rapid acceleration of his aircraft caused localized pain, and more significantly, blurring of vision. Both disturbances were relieved by cranioplasty.

It seems apparent to us, after two years of experience in these problems that the important and realistic indication for the repair of a skull defect in military personnel is the simple existence of such a defect over three centimeters in diameter. In personnel who will not return to duty because of a coexisting cerebral injury, the form of cranioplasty to be described is carried out in the hope of alleviating in every possible way the effect of the initial injury.



FIG. 4—Case 1. Roentgenograms of tantalum plate inlayed in bifrontal defect and early postoperative cosmetic result. The broad scar of the original injury may be removed at a later date.

Materials Used for Cranioplasty—Cranioplasty, being an operation essentially in the domain of plastic surgery, has been favored by the application of much surgical ingenuity in the use of many substitute materials. Its history has been described by Giant and Norcross and reviewed recently by Reeves.⁷ Both papers have noted the use of such substances as animal bone, celluloid, aluminum, gold, the fabled silver plate, platinum, autogenic and heterogenic bone, cartilage, sliding grafts of cranial bone, decalcified bone, buttons of bone and chips of bone. A modern innovation in the use of bone chips and whole blood has been recorded by Converse, Clarke and Guidi.⁸ There appears to be little doubt that until the appearance of certain alloplastic substances, autogenous bone derived from the adjacent cranium, the ilium, the ribs or other osseous structures, was the material of choice for cranioplasty. However, the plastic repair of extensive defects was not always feasible with the use of autogenous bone and the method suffered from the necessity of a second and frequently major operative procedure designed to secure the graft.

The use of alloplastic substances for the repair of skull defects received impetus by the reports of Geib,⁹ Beck¹⁰ and Paxton and Hall,¹¹ describing the clinical advantages of the tissue-merit alloy, vitallium. Its wide application in cranioplasty has been deferred by the fact that vitallium plates must be cast and are not amenable to any degree of secondary adjustment. The use of vitallium implies a two-stage operative procedure and this and other defects in the technic have been answered only partially by Beck's employment of vitallium strips cast in various and perhaps standard sizes. The clinical use of zirconium, whose experimental reactions in tissue have been described by Campbell, *et al*,¹² has been deferred by the onset of the war.

The use of certain synthetic resins has shown distinct, but as yet unproven, promise in cranioplasty. Certain resins appear quite inert in tissue,¹³ and among these is methamethylacrylate (plexiglass). Guidjian



FIG 5—Case . Left frontal supra-orbital and orbital plate skull defect from shell fragment injury

has reported a single, but significant, instance of its use in the repair of a skull defect following removal of a meningioma.¹⁴ Sheldon has used it successfully in his series of studies upon head injuries, marked by observation of the living brain through an acrylic skull plate.¹⁵ Cameron and Elkins¹⁶ have completed some 30 cranioplasties with methamethylacrylate and their results, to be published shortly, may reveal a new chapter in cranioplasty.

The Use of Tantalum in Cranioplasty—In September, 1942, one of us (R. G. S.) performed the first cranioplasty with tantalum in the Walter Reed General Hospital. This clinical trial followed the experimental observations of Burch and Carney,¹⁷ Burke,¹⁸ and Pudenz,¹⁹ and the early clinical trial by Fulcher.²⁰

These studies demonstrated the existence in tantalum of the two essential features of any material used for skull defect repair. In the first place tantalum is relatively inert in tissues and may be considered absolutely inert for all practical purposes. A thin, translucent connective tissue capsule does appear

about this element, well known to military surgeons who have explored peripheral nerve lesions protected by another form of tantalum—tantalum foil. This apparently nonprogressive connective tissue reaction was described by Pudenz,¹⁹ and has been noted also by Pudenz and Odom,²¹ and by

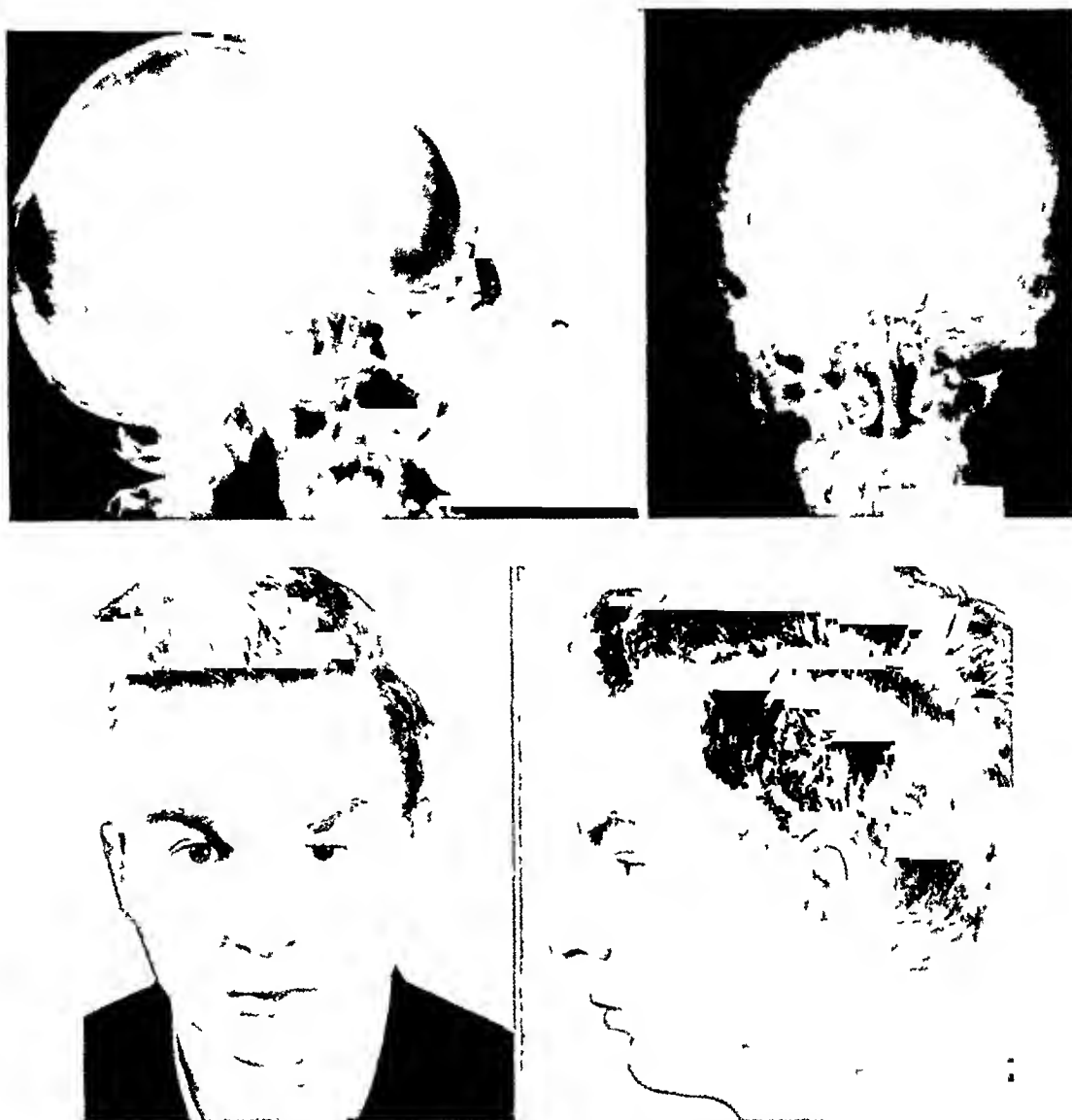


FIG 6—Case 2. Roentgenograms of tantalum cranioplasty and cosmetic restoration after insertion of orbital prosthesis.

Delaiue, *et al*²² In our series of cases, there has been no clinical evidence of tissue reaction to the insertion of tantalum plates, some of them massive in size. No reactions to heat, cold or electrical fields have been a source of complaint to our patients. Pudenz has described proliferation of bone beneath the tantalum plates in his experimental animals. We have had no opportunity to study such a plate after its insertion and the reaction of tantalum to the roentgen ray precludes roentgenographic study of new bone formation.

The second, and desirable, feature of tantalum is its malleability without loss of strength. Flat sheets .015 or .020 inches in thickness and six inches square are available in the neurosurgical centers at this time and larger sheets may be obtained if necessary. The ductility of this bluish-white

element, the 72nd in the periodic table, allows it to be drawn into wire, rolled into sheets of various thicknesses, or formed into structures such as bone plates, ribbon or screws. Its strength may be considered comparable to steel. Whether formed by preoperative molding in a dye and counterdye

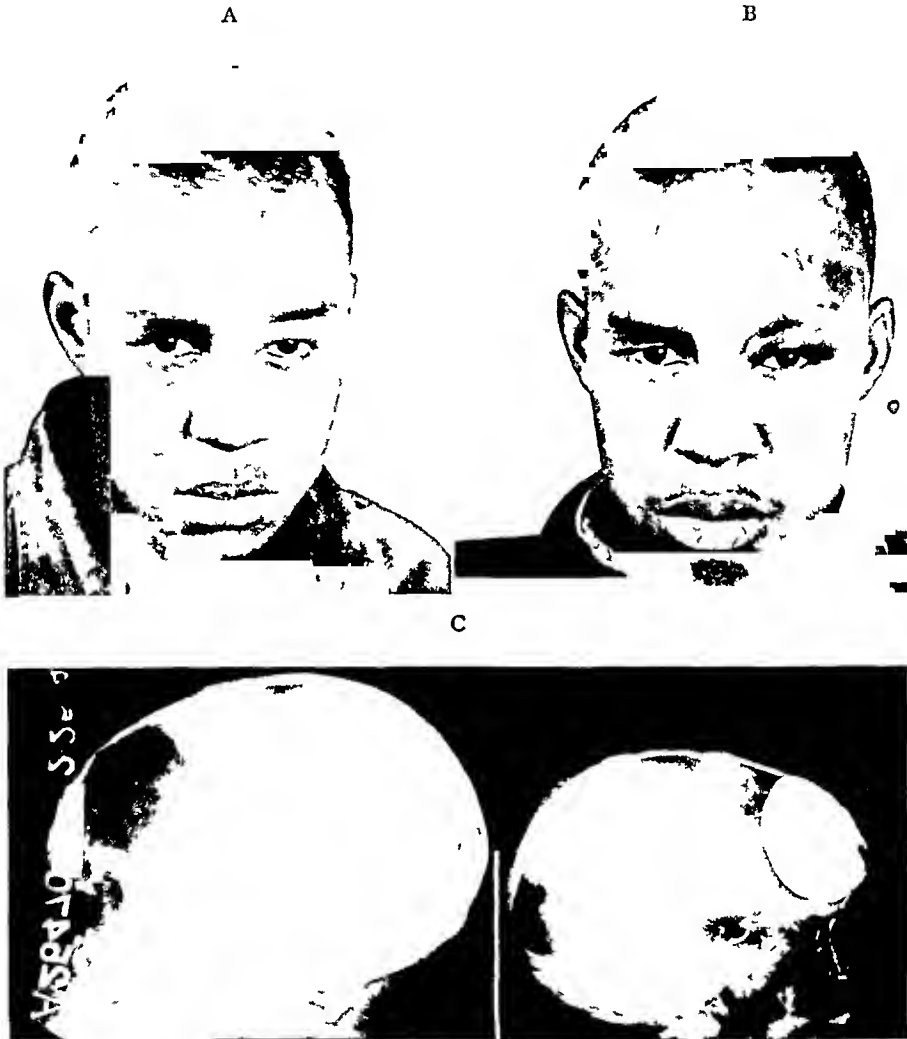


FIG 7—Case 3 (A) Skull defect following resection of osteomyelitic bone
(B) Same patient following tantalum cranioplasty

FIG 7—Case 3 (C) Roentgenograms of skull defect and tantalum repair

or by rough molding at the operating table with a hammer and rounded form, this inherent malleability allows adjustment by cutting or contour changing at the time of operation and, thus, dispenses with multiple operative procedures.

The Preparation of a Tantalum Plate—Indirect or Primary Method— One of the several technics evolved for the preparation and insertion of tantalum plates has been described by Hemberger²³. With the exception of early exploratory efforts in this type of cranioplasty, we have adhered to this technic in the remaining cases of our series. Briefly stated, the method is as follows:

After removal of the long hair, the margins of the skull defect are palpated through the scalp and delineated with an indelible pencil. Dental compound is softened in warm water and molded into the defect and for a considerable distance upon the surrounding scalp. A model is formed by pouring dental stone or plaster into the mass of hardened dental compound and upon this cast, the mark of the indelible pencil will persist. The depressed area within the cast, representing the depth and extent of the bone defect, is filled with wax and contoured to fit the surrounding scalp outline. In complicated frontal defects, this temporary wax prosthesis may be placed in the actual skull defect, in a supra-orbital defect for instance, and compared roughly with the opposite side. In the infrequent deforming bilateral defects, the wax restoration may be studied for verisimilitude by the patient or by relatives. In the uncomplicated defects of the vault of the skull, the convexity of the wax-fill should be overemphasized to compensate for the customary thinning and scarring of the overlying scalp and for the subsequent slight inlay of the plate. A mold is next made with any of the molding sands, including the wax restoration and an ample mass of the adjacent skull contour. A dye is poured with zinc oxide in larger defects with hydromite. The surface of the dye, after cooling, is painted with a solution of alcohol and talc. A soft clay, such as moldine, is adapted about the circumference of the zinc dye to act as a mold for a counterdye of poured lead. The same procedure is followed when hydromite is used. The required size of 0.15 inch tantalum plate is roughly fashioned with at least a one centimeter greater diameter than assumed necessary to compensate for the varying convexity of the plate and for possible enlargement of the bony defect at the time of operation. The plate is swedged between dye and counterdye with a hand or hydraulic press. In the swedging of large and complicated plates, the flow of the element under pressure may be associated with kinking or furrowing. Local adjustment of such changes by hammering will allow completion of the press in successive stages. After the initial press, the edges of the plate are smoothed with carborundum and it is polished with an abrasive disk. A single hole is bored in the proposed dependent portion of the plate or in its central portion for drainage purposes and the plate is reswedged. We have had no experience with plates prepared with multiple perforations but have not used this minor variation in preparation of the plate for fear of causing undue fixation of the scalp to the underlying plate. The proposed use of stainless steel wire mesh²⁴ for the repair of skull defects may be mentioned at this time, since it makes use of a similar principle of multiple perforations. Before use, the plate is cleansed in laboratory cleansing fluid, washed in running water and sterilized in an autoclave. The materials and apparatus required for the formation of such plates are available in any dental laboratory and the skill and experience of Army dental officers in these matters have been of considerable aid in the treatment of the patients reported in this paper.

Operative Fixation of the Plate—The majority of our operative pro-

cedures have been undertaken under local anesthesia, and the required lining and chiseling of bone has been well tolerated with the aid of heavy sedation consisting of nembutal grains $1\frac{1}{2}$, 90 minutes before operation and morphine grains $\frac{1}{4}$ and atropine grains $\frac{1}{150}$, 30 minutes later. In unilateral and bilateral frontal defects, the use of a coronal scalp flap and manipulation about the frontal sinus and orbit have demanded the use of a general anesthetic, in these cases intratracheal ether. Insertion of the plate is facilitated by placing the area of skull defect on a horizontal level and full use of the cerebellar frame, and other adjuncts to such posturing, is advocated.

Among the 79 skull defects repaired, 62 were caused by direct enemy action and the definitive treatment of the acute injury was carried out by overseas neurosurgeons. In 54 of the 62 injuries, the resulting scalp scar was represented by a linear scar of varying length. Tripod or formal craniotomy scars were rarely observed, there were five of the former and three of the latter. The skull defects were uniformly oval or rounded and no defects were characteristic of formally resected areas of bone, advocated in World War I. The predominance of linear scars allowed approach to the skull defect in most cases by simple excision of the original scar, and by dissection and retraction of scalp flaps. In temporal bone defects, the usual craniotomy incision making complete or partial use of sagittally directed scars and circumscribing vertical scars is indicated since the mass of muscle and the increased vascularity following injury in this region makes direct exposure of the defect unnecessarily difficult. In frontal defects, rostral to the hair line, coronal incisions are used. Plastic revision of broad or deforming frontal scars may be done as a secondary procedure. In the rare tripod scars, exposure of one angle of the former incision may be sufficient for insertion of the plate. Cranioplastic incisions about a horizontal scar should be avoided since they will be followed by incision line necrosis. The revision of broad thin scalp scars, adherent to underlying brain tissue demand special study and may present formidable problems.²⁵ Typical scalp scars, defects and cranioplastic incisions are illustrated (Fig. 2).

After adequate exposure of the area of the skull defect, its edges may be readily palpated. An incision is made through the pericranium about the edge of the defect one centimeter from its margin. This pericranial tissue is resected centrally, together with any excess extradural tissue over the area of the defect. Indicated bone resection, cerebral scar resection, dural repair, or other measures, are carried out. To initiate the insertion of the tantalum plate, it is held provisionally over the defect and its margin altered if necessary with heavy cutting scissors so that it overlaps the margin of the

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- A—Bifrontal skull defect from aerial torpedo fragment wound
 - B—Lateral view of bifrontal skull defect
 - C—Coronal scalp incision used for exposure of defects rostral to hair line
 - D—Exposure of skull defect after resection of pericranium about defect
 - E—Preparation of circumferential ledge about defect prior to insertion of plate
 - F—Fixation of tantalum plate by means of tantalum wedges
 - G—Completed operative procedure
 - H—Frontal view of patient after tantalum cranioplasty
 - I—Lateral view of cranioplasty. Note restoration of frontal bone contour

PLATE I



A



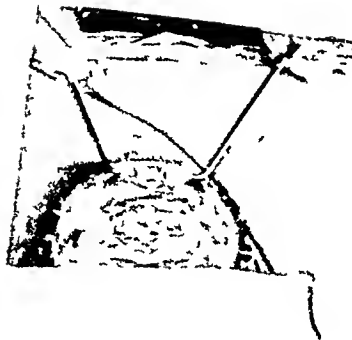
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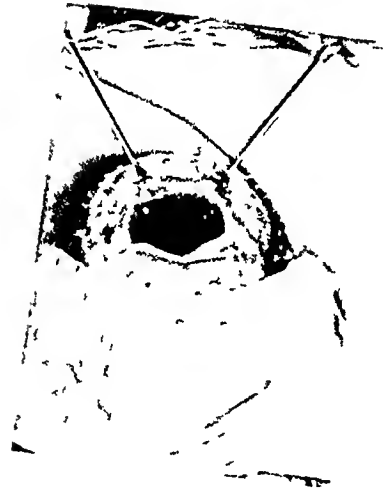
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H



I

defect for an approximate distance of one-half centimeter. This border is then marked by an ordinary dental scaler and cut to a depth of two millimeters with the lineator, one of the simple instruments designed by Hemberger for this procedure. This incision into bone, at right angle to the surface of the skull forms the sharp inner border of a circumferential ledge about the border of the defect, one-half centimeter wide and two millimeters deep, formed by a Stout No. 3 dental chisel. The preformed tantalum plate is then fitted into this ledge, its upper border flush with the skull, necessary adjustments being made with cutting scissors or minor contour changes with a contour pliers. With the plate held in position by digital pressure, fixation is secured by means of tantalum triangular points, much like glazier points. Seats for the tantalum wedges in the outer border of the bony ledge are made with a triangular pointed instrument, the perforator. The tantalum wedges, made of 0.20-inch plate, are tapped into place in the bone, and turned inward over the edge of the plate with a wedge director. Four to six tantalum points may be used in any one case. In plates assuming a vertical position, front or occiput, wedges may be driven through a drill hole in the superior margin of the plate and the weight of the plate suspended in this manner. Following insertion of the plate and closure of the scalp, a firm, evenly distributed pressure dressing is applied, preferably with one of the new adhesive dressings, such as Nuhesive. Such a dressing decreases the number of postoperative aspirations of fluid blood which may collect in spite of meticulous hemostasis. Cranioplasty in this series of cases has been undertaken as soon as primary wound healing has occurred and has not been deferred because of a history of preexisting cerebral infection. Prior to operation, prophylactic penicillin therapy is instituted with 30,000 units of penicillin being given every three hours for the 24 hours prior to operation. At the termination of the cranioplasty, 30,000 units are injected beneath the scalp incision (10,000 units/cc) and 15,000 units are given every three hours intramuscularly for the following three days. Two postoperative infections developed prior to the institution of this therapy, both in postinfection cases, both were controlled without open drainage and without loss of the inlayed plate. There have been no infections under the regimen outlined above. There have been no other postoperative complications of significance.

Preparation and Insertion of Tantalum Plate—Direct or Secondary Method—The method which has been described is applicable to the majority of the skull defects observed some time, *i.e.*, two to four months, following the initial injury. An important variation, which may have a wider application in the field of civilian neurosurgery, consists of a preliminary direct impression of the proposed tantalum plate, and its insertion at a secondary operation. The débridement of bone in acute injuries of the skull, or the removal of a skull tumor, or the sacrifice of a bone plate at craniotomy, may suggest the desirability of a secondary repair of the resultant skull defect. In suitable cases, this repair may be facilitated by ledging the circumference of the bony defect as described previously. An impression is made of the

extent of the bony defect and the exact contour of the circumferential ledge with autoclaved dental compound. Prior to closure of the primary incision, a sheet of tantalum foil, .00025 inches thick, is placed over the defect and extending well beyond the ledge. Repeated experience with this method has shown that this is an important step in this technic of repair, since at the secondary operation for the insertion of the plate, the skull defect and adjacent bone will be found uninvolved in scar tissue and not adherent to the overlying scalp. The tantalum plate, formed from the direct impression will need no adjustment at secondary operation and the procedure may be carried out expeditiously at any time deemed advisable during convalescence (See Case 2)

TANTALUM CRANIOPLASTY IN FRESH WAR WOUNDS

In addition to the more refined methods of cranioplasty that have been described, other methods are available for the repair of skull defects involving relatively uncomplicated skull contours. These include the preforming of plates upon a basic model of the skull, with the only individual variation being the size of the plate, the "hammering" of plates with the aid of preformed plaster molds and the preparation of plates at the operating table by "hammering." Fixation methods include the simple onlay of the plate or inlay of the plate in a ledge, springing of the plate in a ledge,²⁶ wiring,²³ or minor variations in the preparation of the ledge or the use of V-shaped prongs formed as part of the plate and driven into the outer table of the skull as a method of fixation. None of these methods is applicable to the repair of deforming, complicated frontal defects.

Onlay tantalum plates, secured with wire sutures, or inlay plates secured with tantalum wedges, with the plates hammered out at the operating table, may have a place in the cranioplasty of fresh war wounds, and the principles involved may be used in fresh civilian wounds of the skull. Immediate cranioplasty of this type is only possible because of the lowered incidence of infection secondary to penicillin therapy and should be reserved for those cases without dural penetration. This procedure must still be considered to be in a stage of clinical trial, representing one of the efforts to hasten the convalescence of military casualties. The following case report illustrates a pioneering effort in this direction.

Case 4—Reg No 219533, Walter Reed General Hospital. R. W. D., age 21, was injured in France at 1030 hours, July 26, 1944, by the tree-burst of an 88-millimeter shell. He sustained a penetrating wound of the vertex of the skull, the shell fragment traversing his helmet and causing a compound, comminuted fracture of the left parietal bone adjacent to the sagittal sinus and also involving the right parietal bone. He was unconscious for ten minutes and upon regaining consciousness, noted motor and sensory paralysis of both lower extremities. The right lower extremity improved steadily during the next 90 minutes. Sulfonamide therapy, local and general, was continued during evacuation to England. On July 29, 48 hours after injury, debridement of scalp and bone was performed, with removal of a small extradural hematoma. The dura was intact and was not opened. The outer table of the skull about the circumference

of the bony defect was removed, forming a ledge upon which a "hammered" plate was laid and fixation secured by tantalum points. Penicillin was given locally and parenterally and wound healing was normal.

At the present writing, the patient shows a mild spastic monoplegia, with diminution in cortical sensibility in the left lower extremity. The electro-encephalogram is normal and the cranioplasty is technically above criticism.

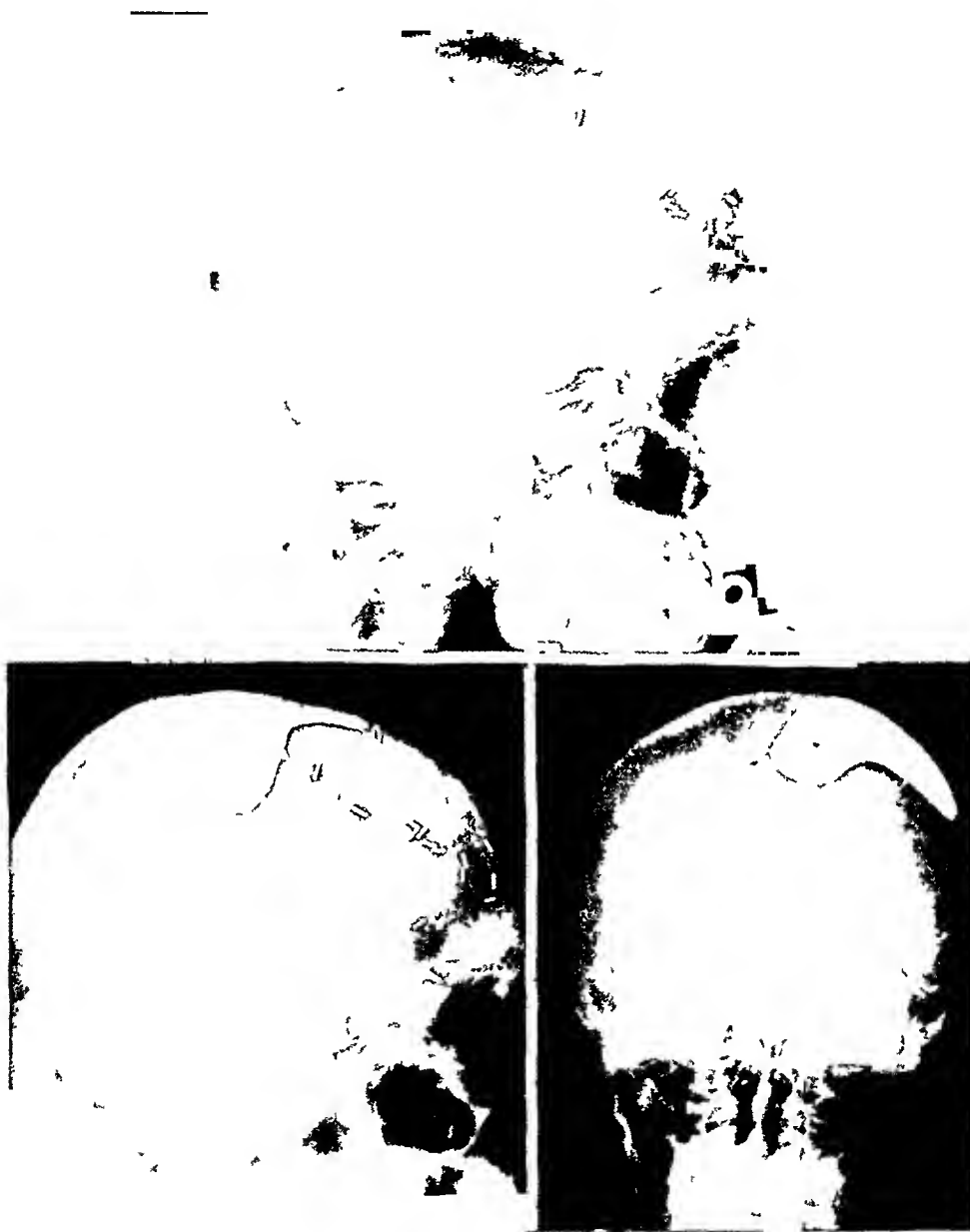


FIG 8—Case 4. Roentgenograms of skull defect following craniotomy for tumor and subsequent tantalum cranioplasty and wire fixation of remaining bone plate.

ANALYSIS OF 79 CASES OF TANTALUM CRANIOPLASTY

In a previous report,²³ several massive tantalum cranioplasties have been reported in an effort to illustrate the utility and simplicity of the operative technic and the facility with which the element may be adjusted to any type of repair. Similar unusual cases have been reported elsewhere.^{7, 26} We wish to emphasize the fact, however, that the majority of skull defects

resulting from war wounds are relatively uncomplicated problems. This fact, added to the essential inertness and malleability of the element and the technical ease of its insertion, makes tantalum cranioplasty a procedure available not only to trained neurosurgeons but to military surgeons as a whole. Pertinent analyses of the cases we are reporting may be summarized as follows:

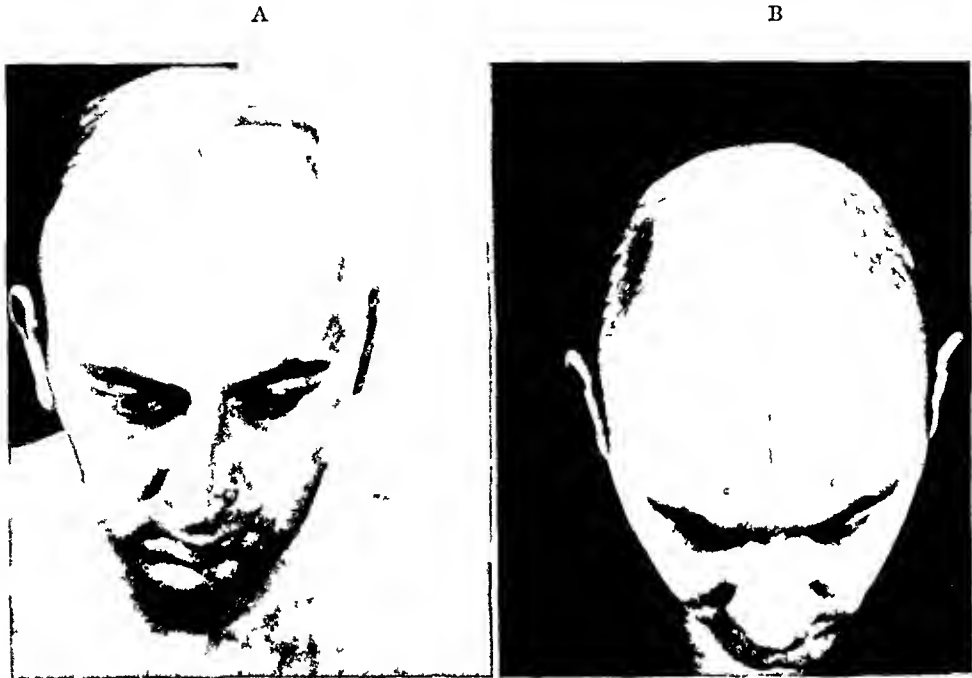


FIG 9—Case 4 (A) Irregular skull defect following craniotomy for tumor (B) Cosmetic result following tantalum cranioplasty

LOCATION OF DEFECT			
Right frontal	12	Left frontal	18
Right temporal	5	Left temporal	6
Right parietal	8	Left parietal	10
Right occipital	3	Left occipital	4
	—		—
	28		38
		Bifrontal	7
		Biparietal	3
		Bioceipital	3
			—
			13

The predominance of left-sided injuries is probably not of statistical significance but in this particular series of cases has exerted some influence on the character of the posttraumatic neural defect.

CAUSE OF INJURY			
Shell fragment	48	Osteomyelitis	2
Vehicle accident	6	Mine explosion	1
Blow	4	Aerial torpedo	1
Rifle bullet	4	Bayonet	1
Machine pistol bullet	3	Propeller blade	1
Machine gun bullet	3	Dynamite explosion	1
Craniotomy	3	Horse kick	1

The majority of skull defects are caused by shell fragments. This fact would suggest a failure to survive the impact of the higher velocity missiles of

rifle and machine gun This point can only be judged with the aid of active theater military pathologists

ASSOCIATED WITH PERMANENT NEUROLOGIC DEFECT

Hemiplegia	9
Unilateral loss of vision	8
Hemiplegia and aphasia	6
Aphasia	5
Bilateral loss of vision	5
Mental retardation	2
Hemiplegia and loss of vision	1
Monoplegia	1
Homonomous hemianopsia	1
	—
	38

The character of the residual neurologic defect, observed at an average time of four months after injury, has been described in rough terms that serve to indicate merely the usual forms of permanent injury, the potential percentage of severe sequelae and their influence upon disposition to duty

INDICATIONS FOR CRANIOPLASTY AND THE RELIEF OF SYMPTOMS

A statement concerning the indications for cranioplasty with particular reference to the influence of the factor of return to duty has already been made We have not analysed in detail local or subjective symptoms presented by our patients We have been impressed, however, by several points that deserve comment

The majority of our patients have noted localized tenderness upon palpation of the area of the defect, and have complained of localized pain that has had a tendency toward spontaneous resolution These subjective complaints have been benefited by cranioplasty Vertigo and generalized headache are less common complaints and appear unaffected by cranioplasty They represent, in all probability, the sequelae of the cerebral injury In the same category rests the complaint of tingling paresthesias in upper or lower extremities and chest wall occasioned by a rapid and pronounced flexion of the cervical spine and unaffected by cranioplasty

The number of repulsive or deforming defects is measured by those involving the supra-orbital and frontal regions of the skull rostral to the hair line When associated with unilateral or bilateral loss of the orbital contents, they represent cosmetic disorders that demand improvement The combination of tantalum cranioplasty and the insertion of appropriate orbital prostheses has given gratifying results

A study of this series of cases has presented at least a partial answer to the problem whether or not any form of cranioplasty may influence an underlying convulsive state Observations of the effect of cranioplasty upon changes in electrical activity of the brain have been made in 26 cases studied before and after cranioplasty over a varying time period from 4 to 12 months Identical records may be obtained before and immediately after tantalum cranioplasty, and it is obvious that the tantalum itself has no

influence upon the technic of this examination. In these 26 cases, 12 showed no subsequent change in the character of cortical electrical activity, in ten there was evidence of improvement in an abnormal electro-encephalogram and in four the abnormal activity became even more manifest, with the development of epileptogenic foci. Cranioplasty was not performed upon patients whose convulsive state had not been controlled by conservative measures and thus far, there has been no opportunity to judge the direct effect of cranioplasty upon an uncontrolled convulsive state. The excision of the concomitant cerebral scar will always invalidate such a trial. Studies upon additional cases have not altered these impressions.

DISPOSITION TO DUTY OR OTHER STATUS

Discharged or retired for physical reasons	
Neurologic defect	28
E E G epileptogenic focus	6
Convulsions	5
Other contributing factors	4
	—
	43
Discharged from hospital to duty	36

POSTOPERATIVE COMPLICATIONS

Infection	2
Plate slipping (early case)	1
Extradural pneumatocele (frontal sinus)	1
	—
	4

The Value of Complementary Pneumo-encephalography—We have not been impressed by the value of pneumo-encephalography in the estimation of the degree of concomitant cerebral injury when compared to the aid derived from a carefully reviewed history, from the neurologic examination and, in particular, from repeated electro-encephalographic studies. Only 18 air studies have been conducted in these patients, the majority in those exhibiting convulsions or an epileptogenic focus. They have added nothing but confirmative evidence to less distressing methods of examination and appear to hold a minor place in the survey of a relatively fresh injury. With the use of multiple projections, the insertion of a tantalum plate, unless it be of massive size, need not detract from the future application of this method, in those cases in which resection of a cerebral cicatrix may be indicated.

ILLUSTRATIVE CASES

Case 5—*Midfrontal defect, aerial torpedo wound on November 27, 1943. Tantalum cranioplasty, indirect, primary method on June 29, 1944. Adequate cosmetic result.*

J. K., Reg. No. 215697, Walter Reed General Hospital, age 32, was injured on a troop transport by fragments from an aerial torpedo. There was no loss of consciousness nor evidence of neurologic defect. He was lowered over the side of his ship and floated about for several hours before being rescued by a friendly mine-sweeper. Debridement and primary closure of a midfrontal, compound, comminuted fracture of the skull with cortical laceration was carried out 48 hours after injury by a British installation. Wound healing was normal. There was no history of convulsions. He was received at this hospital on June 17, 1944. He had no complaints and the neurologic examination was

normal There was an irregular skull defect in the midfrontal region, rostral to the hair line, and involving the medial and superior margins of both supra-orbital ridges, more so on the left Roentgenograms more clearly define the extent of the defect The preoperative electro-encephalogram showed bursts of fast activity, 14-22 per second, in both frontal leads Spinal air injection disclosed a normal ventricular system and subarachnoid space Tantalum cranioplasty through a coronal scalp incision with reflection of the rostral flap disclosed the skull defect A well-contoured, preformed tantalum plate was inlayed in the usual bony ledge and fixation was secured with tantalum wedges An adequate roentgenographic and cosmetic result was obtained (Figs 3, 4 and 5)

This particular defect and the method of repair may be considered as fairly typical of the majority of cases in this series

Case 6—Left frontal skull defect, caused by shell fragment injury on January 6, 1944, associated with loss of left orbital contents and intra-orbital cerebral fungus Meningitis Resection of fungus, dural graft and control of subarachnoid infection Tantalum cranioplasty, direct, secondary method, on June 1, 1944, and transfer to Ophthalmological Center

L P D, Reg No 213526, age 22, was struck by shell fragments in the left frontal region and in the left orbit on January 6, 1944 He was semicomatose for the first 24 hours and during this time the left orbital contents were everted and a compound, comminuted fracture of the left frontal bone, frontal sinus and orbital plate was débrided and closed His convalescence was smooth and after return to the Zone of the Interior, he was sent to an ophthalmologic center for an orbital prosthesis On May 7, he developed fever, cervical rigidity and rapidly became stuporous Lumbar puncture demonstrated a sterile pleocytosis of 835 cells, half of which were polymorphonuclear in type The acute meningeal infection was controlled readily with daily injections of 10,000 units of penicillin in the lumbar subarachnoid space Review of the overseas record suggested the possibility of an intra-orbital cerebral fungus On June 1, 1944, a coronal scalp flap was reflected rostrally exposing the bony defect A yellow, scarred mass of necrotic cerebral tissue filled the orbit This mass of tissue was resected until the margins of a triangular dural defect were visualized An appropriate-sized area of pericranium was placed over the defect and held in place by a thin disk of fibrin foam, impregnated with penicillin The customary ledging of the edge of the bony defect was made, the mold for the proposed tantalum restoration taken, and the defect and the adjacent ledge were covered with tantalum foil, .00025 inches thick The coronal flap was then closed with galeal and scalp interrupted sutures of fine nylon

Twenty-five days later, the former coronal suture line was reopened and the protecting tantalum foil removed The operative field was quite clear of scar tissue and not adherent to the scalp Tantalum cranioplasty was promptly accomplished This patient has been returned to an ophthalmologic center for plastic revision of the eyebrow and upper lid and for the orbital prosthesis to complete his rehabilitation (Figs 6 and 7)

Case 7—Frontal sinusitis, left, on August 26, 1943 Extradural abscess, osteomyelitis; left frontal bone Left frontal brain abscess Resection of brain abscess in December, 1943, after previous resection of left frontal bone Recovery with tantalum cranioplasty on March 2, 1944

C B, Reg No 200710, Walter Reed General Hospital, age 23, while training, developed an acute left frontal sinusitis on August 26, 1943 Drainage of this infection was followed by osteomyelitis of the left frontal bone and an extradural abscess Resection of the involved bone was carried out on September 21, 1943 His convalescence was protracted, and following the development of stupor and electro-encephalographic localization of a focus in the left frontal lobe, an intracerebral abscess was at first aspirated and later enucleated in December, 1943 All procedures were protected by

penicillin administered by appropriate routes. On March 2, tantalum cranioplasty restored the normal skull contour of the left frontal region (Fig 8).

Case 8—*Craniotomy for left parasagittal tumor on December 3, 1943. Postoperative infection controlled by penicillin, with partial loss of craniotomy flap. Convulsive state,*



FIG 10—Roentgenograms of multiple skull defects following operation for subdural hematoma and following subsequent tantalum cranioplasty.

with marked anxiety concerning pulsating defect. Tantalum cranioplasty on June 29, 1944, with relief of subjective disturbances and mental rehabilitation for reentry into civilian status.

H M F, Reg No 214687, Walter Reed General Hospital, age 31, developed headache, vomiting, impairment of vision, indifference and slow cerebration while overseas, with rapid progress of symptoms and neurologic signs suggesting a left frontal lobe tumor.

A technically difficult resection of a left frontal lobe parasagittal meningioma was accomplished on December 3, 1943, necessitating further bone resection for exposure of the tumor. His convalescence was interrupted by a wound infection, readily controlled by penicillin. An intermittent convulsive state was aided with conservative measures following his evacuation to the Zone of the Interior. There was an extensive frontal alopecia and the patient developed an anxiety state, centered upon the obvious deformity and the fear of injury to the pulsating defect. On June 29, 1944, tantalum cranioplasty corrected the deformity and stimulated favorably his rehabilitation to civilian status. Restoration of much larger postcraniotomy defects have been reported^{7, 26} (Figs 9 and 10).

Case 9—Blow in right temporal region on February 14, 1943. Gradual onset of increasing intracranial pressure with evacuation of a chronic subdural hematoma on March 30, 1943, through a subtemporal decompression opening following two exploratory trephines. Tantalum cranioplasty on September 7, 1943.

D. A. A., Reg. No. 198922, Walter Reed General Hospital, age 24, was struck with a beer bottle in the right temporal region on February 14, 1943. He sustained a closed head injury and was unconscious for two days. His recovery was protracted and never complete. He continued to complain of headache and developed diplopia, left-sided motor weakness and papilledema. On March 30, 1943, a chronic subdural hematoma was evacuated in another hospital. Following a smooth convalescence, he developed pain in the pulsating skull defect. Spinal and injection studies and electro-encephalography were normal. On September 7, 1943, a gooseneck tantalum plate was inserted effectively protecting the irregular decompression opening and a tender rather large, frontal trephine opening (Fig. 11).

A minor technical point is to be noted in the accompanying illustration. The thin squamous portion of the temporal bone does not allow wiring readily nor does it permit ledge formation. In this area, primary fixation of a tantalum plate may be obtained by alternating small, V-shaped wedges of the plate itself, implanted above and below the bone edge. The remainder of the plate is then fixed by any of the methods described.

CONCLUSION

Tantalum cranioplasty has been carried out in 79 skull defects occurring in Army personnel as a result of war wounds and casual injuries. Tantalum possesses two qualities essential for a cranioplastic material, inertness in tissue and strength associated with malleability. Defects involving complicated contours such as those of the supra-orbital ridge are best repaired by the use of preformed plates. The technic of inlay of the plate into a circumferential ledge and fixation by means of tantalum wedges is a simple procedure, widely applicable throughout all Army surgical installations.

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DISCUSSION—DR W J MIXLER, Boston, Mass I have seen a good deal of this work and, as I see it, the use of the tantalum plate is a great advantage to the men in the armed forces There is no question but what there will be many of these plates used in this war, and we must consider what are the limitations of the procedure and what are its advantages over bone graft, and what is going to be the ultimate result to the patient In the first place, these plates, particularly if preformed, and particularly if handled in a service which is set up for it, are easy of application The first one you use in your civilian hospital, never having done this before, will take a long time and you will sweat over it, but after you achieve the technic you will find that you have something so much better and so much easier to handle than grafts that there is no comparison

As to the limitations of this procedure, I think we will all agree it is very valuable in large defects, but the question arises how far it should be carried in small defects. In civilian life we have paid little attention to many of these small defects. However, in the Army, by using a plate, perhaps two centimeters in size, you can make the patient effective for service, perhaps limited duty, perhaps combat duty. The effect on morale is great. The difficulty will be not in persuading patients to have them put in, but in refusing to put them in for patients who do not need them.

LT COL D HENRY POLR, Newton D Baker General Hospital, Martinsburg, W Va. In discussing this most interesting paper I would like to present a preliminary report of the methods being used at the Newton D Baker General Hospital in dealing with cranial defects. This work is being carried on by Major Charles W Elkins, of Cleveland, and his associates, and their results have been highly satisfactory.

Since all substances used for cranioplasties are known to have some disadvantages, a more satisfactory one was thought to be necessary and desirable. Since a resin polymer, known as methyl mercrylate or acrylic, could be readily moulded into the desired shape, size, and contour and, being nonmetallic, was not subject to the physical effects incident to changes in temperature, or effects of electrical phenomenon, this substance was selected. Up to the present time, 39 patients have been operated upon without infection or other complication. In the patients requiring accurate maintenance of bone contour such as reconstruction of the supra-orbital ridge, and the nasal bones, a particularly desirable result was obtained. Convulsive seizures followed operation in two patients, but these are in no way considered to be influenced by the substance used for closure of the defect. The largest elapsed time since the earliest implantation is approximately 14 months (Case of Major Joseph Cameron), and there has been no untoward reaction in the tissues. Requiring close cooperation with the dental laboratory, when these moulds are made, it is now possible to perform the entire operation in one stage, using local anesthesia.

It is our thought at the present time that acrylic, or lucite, has certain definite advantages over tantalum, and other materials being used for cranioplasties.

DR CLAUDE C COLEMAN, Richmond, Va. It is interesting to note the changed attitude toward cranial defects. In the early days of surgery for brain tumor, and other expanding lesions, cranial defects were made to give relief of intracranial pressure. The removal of bone in the temporal region, known as "subtemporal decompression" was formerly the principal operation both for tumor and for trauma. Cranial defects, therefore, were not looked upon with any particular disfavor. At the present time the tendency is to keep cranial defects to a minimum and to repair those that are inevitable. In World War I, the repair of defects was the chief cranial operation and there seems to be even more enthusiasm for repair of cranial defects in the present war. It may be this enthusiasm is not entirely justified.

I have been very much interested in tantalum as a material for the repair of cranial defects but until recently this material was not available, and I have had no experience with it in cranioplasty. In the years between the two World Wars, I used celluloid plate and, in my experience, this material for cranioplasty has been entirely satisfactory.[†] I could not expect better results from any other material. Celluloid is easily molded and thus far I have found it necessary to remove only one plate because of infection. In this case the defect involved the frontal sinus and sufficient time had not been allowed for the patient to recover from the primary infection. The use of celluloid for repair of cranial defects was brought to the attention of this Association by Dr W P Nicolson at a meeting in Pinehurst in 1920.

It appears that the trend now is definitely against autogenous transplants, although a transplant from the outer table of the skull was widely used for repair of cranial defects in World War I. This method, used in army cases at Cape May, was described by me in 1920.[†] Dr Joseph E J King used grafts from the tibia with satisfactory results.

[†] Horsley and Bigger. Operative Surgery. Vol 2, 4th Ed, p 1199, St Louis, C V Mosby Co, 1937.

[†] Coleman, Claude C. The Repair of Cranial Defects by Autogenous Cranial Transplants. Surg, Gynec & Obst, 31, 40, July, 1920.

To procure autogenous transplants is a considerable operation, particularly if the outer table of the skull is used. The procedure for obtaining such transplant may be harmful to the patient, requiring as it does a good deal of hammering on the skull.

I dislike to make too many references to the First World War, because I understand I am slated for the Senior List of the Association, however, some reference might be made to what were considered indications for cranioplasty in 1919. All indications were subjective except in those defects which caused conspicuous deformity. The principal complaints of these patients arose from fluctuation of the brain mass through the defect on changing position of the head. This fluctuation caused disagreeable sensations of the head which cranioplasty relieved. It was not believed by those who had experience in World War I that the repair of cranial defects prevented or favorably affected convulsions. Repair of a defect gave a feeling of protection and a sense of security. However, the very small defects, unless producing a deformity, were not repaired. It seems that the indications now for cranioplasty are based largely on the patient's desire for operation. The fact that he desires it seems to be sufficient indication for its performance.

Many cranial defects in civilian practice can be prevented. In all simple depressed fractures of the skull the bone fragments may be replaced and in many compound, depressed fractures if there is not too much contamination and when the operation can be undertaken early.

I was very fortunate in having the opportunity to see some of the cranial defect work at Walter Reed, and other army hospitals. The results of cranioplasty with tantalum plate in the hands of Major Woodhall and others appear to be excellent.

DR JOSEPH E. J. KING, New York, N. Y. I am happy to hear this paper, and to see the splendid results. The use of tantalum plate has a decided advantage over anything we have seen heretofore. Vitallium was difficult to mold and get into shape, and we could do little with it and, therefore, have discarded it. I think this has a decided advantage over any material except probably the celluloid used by Coleman in the enormously large defects that extend in different directions, because you cannot obtain any living transplant to fit well into such defects. As to small defects, I have not seen any objection to the autogenous grafts, except that they are not so easily molded. I have never seen one lost, nor seen any failures since we have used the tibial grafts instead of the thin ones from the outer table, which become absorbed and disappear. I do not think these defects should be repaired if there is any possibility of underlying infection, or in or about the frontal sinus unless the entire sinus has been totally obliterated. I cannot accept putting either bone or metal in unless all mucous membrane and cavity have been eliminated. With missiles buried in the brain I see no point in performing any type of cranioplasty unless the foreign body is removed.

Several years ago, Dorothy Klenke removed the bone from a flap in the first stage of an operation for what was thought to be a malignant underlying tumor. But when she opened the dura a few days later it proved to be a meningioma. So there was a large defect. One of the boys remembered he had taken the bone over to the laboratory, so he brought it back. She perforated it several times in a pepper-box manner with a small drill, put it back in place, and had perfect healing—with bone that had been discarded four days before.

In osteomyelitis, as shown by Furstenberg, and others (and in my personal experience), there is no need of repairing these postoperative defects if the dura is intact and the pericranium has been turned down and is later approximated against the dura. I have never seen one that failed to repair itself in two or three years, more rapidly in children than in adults.

DR JOHN W. PRICE, JR. Louisville, Ky. I cannot resist the temptation to express my appreciation of this splendid work that is being done by neurosurgeons in this war. As one of Doctor Cushing's boys in the last war, I feel that I can speak with some authority on what we had. I did the brain work in Evacuation Hospital No. 7 and No. 15, and in the mobile hospitals, and what Major Woodhall said about these defects being the result of mine accidents principally, and not machine gun bullets, bears out our experience. We did not have so many cases come back to the United States after they got into our evacuation hospitals, yet a few did come back. But the marvelous

work this group is doing today I think is a monument to the early training of the brain surgeons, which has been going on for the past forty years.

DR AITON OCHSNER, New Orleans, La. This marvelous element was first worked on by John Burch, a member of the Southern Surgical Association, at Vanderbilt University. So I think we should be proud of him.

I would like to ask whether there is any danger of heat absorption from the implantation of this metal. There have been some reports of this.

MAJOR BARNES WOODHALL, Washington, D. C. (closing). We have invested a considerable amount of the well-being of our soldiers in this type of cranioplasty. Some of our colleagues in other fields of endeavor have carried out intensive studies on the influence of cold and heat and electrical fields upon these plates. So far as I know, individuals with tantalum plates do not react adversely to these influences under normal conditions of living. However, we would be derelict in our duty if we did not have another type of cranioplasty up our sleeves, as it were, in case tantalum cranioplasty should fall down under some unforeseen influence. I am, therefore, grateful to Colonel Poer for discussing acrylic cranioplasty. We have seen the majority of cranioplasties turned out by this method and there is no doubt but that the cranioplasty, so far as results are concerned, is beyond reproach. I feel, however, that the technic is more difficult in complicated cases and, in addition, the synthetic resins are not malleable and a two-stage procedure is always necessary.

In response to Doctor Coleman's remarks, may I say that the neurosurgical centers would be greatly weakened if we did not have the constant aid and comfort of what he calls the senior neurosurgeons.

PENICILLIN AS AN ADJUNCT TO THE SURGICAL TREATMENT OF ACUTE AND CHRONIC EMPYEMAS*

LT COL BRIAN BLADES, M C , A U S

WASHINGTON, D C

FROM THE THORACIC SURGICAL SECTION, WALTER REED GENERAL HOSPITAL WASHINGTON D C

THE INTRODUCTION of any therapeutic agent which may control infections is received with enthusiasm by both surgeons and internists. The former anticipates reduction and perhaps elimination of postoperative infections. The latter hopes that surgical intervention will no longer be necessary.

The astonishing results which have been obtained with penicillin have naturally revived interest in the nonsurgical treatment of empyema and also stimulated investigations on the value of the agent as an adjunct to surgery.

Optimistic reports are already recorded in the literature on the treatment of postpneumonic empyema by local and systemic administration of penicillin. For example, Tillett, Cambier and McCormack¹ report eight cases of pneumococcal empyemas treated by intrapleural injections of penicillin. In seven, the infection was eliminated, six patients recovered completely, and only one patient was operated upon. Keefer² and his associates have recorded successes in sterilization of empyema cavities by local penicillin therapy. Bennett and Parkes³ describe four more penicillin cures of empyema, and are hopeful that the necessity of surgery for suppurative pleurisy will be largely eliminated by the use of penicillin. Undoubtedly, as penicillin becomes generally available, more successful nonsurgical cures of empyema will be described.

PENICILLIN IN THE TREATMENT OF ACUTE POSTPNEUMONIC EMPYEMA

Twenty-four patients considered to have acute empyema and originally treated with penicillin have been studied on the Thoracic Surgical Section, Walter Reed General Hospital. Twenty-one of these cases were transferred to a general hospital after treatment was begun. The amount of penicillin given, the methods of administration and the time factors varied considerably in this group. Thirteen patients received both intramuscular and local penicillin therapy. Six patients received systemic administration of the drug alone. In five cases, only local penicillin therapy was employed (Tables I, II, and III). The bacteriologic details are not important except to state that in all but two cases the infections were caused by penicillin-vulnerable organisms.

Penicillin Cures—Three patients escaped drainage operations. In one case only intramuscular penicillin was given. Both intramuscular and intrapleural routes of administration were employed in the other two patients who recovered without surgical intervention.

* Read before the Fifty-sixth Annual Session of the Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

Critical analyses of these cases reveal that in two patients in whom repeated aspirations and penicillin therapy were credited with effecting a non-surgical cure of empyema, the fluid was infected but did not thicken to form gross pus. It is obvious, therefore, that a true abscess had not formed and the empyemas were not cured but were aborted.

TABLE I

COMBINED SYSTEMIC AND LOCAL PENICILLIN—13 CASES

Pleural fluid sterile	10 cases
Penicillin cures	2 cases
Chronic empyema	1 case
Thoracostomy	11 cases

RESULTS IN 13 CASES OF ACUTE POSTPNEUMONIC EMPYEMA TREATED WITH BOTH INTRAMUSCULAR AND INTRAPLEURAL PENICILLIN INJECTIONS. ELEVEN REQUIRED SURGICAL DRAINAGE.

TABLE II

INTRAMUSCULAR PENICILLIN—6 CASES

Pleural fluid sterile	2 cases
Penicillin cure	1 case
Chronic empyema	1 case
Thoracostomy	5 cases

RESULTS IN SIX CASES OF ACUTE EMPYEMA TREATED WITH INTRAMUSCULAR PENICILLIN ALONE. IT IS INTERESTING THAT THE PLEURAL FLUID BECAME STERILE IN TWO CASES.

TABLE III

LOCAL PENICILLIN—5 CASES

Pleural fluid sterile	5 cases
Chronic empyema	1 case
Thoracostomy	5 cases

A SUMMARY OF THE RESULTS IN FIVE CASES TREATED WITH ONLY INTRAPLEURAL INJECTIONS OF PENICILLIN. THE PUS IN THE EMPYEMA CAVITIES BECAME STERILE IN ALL CASES BUT THICKENED AND REQUIRED SURGICAL DRAINAGE.

In only one "penicillin cure" thick creamy pus was found in the pleura. Cultures revealed *beta Streptococcus* and *Staphylococcus albus*. Intrapleural injections of penicillin were given over a period of 24 days with two initial doses of 100,000 units followed by three injections of 40,000 units. Cultures of the pus were sterile after the first injection of penicillin. Over 5,000 cc of pus was removed by aspiration. Eleven thoracenteses were performed. Intramuscular penicillin therapy was continued for five months. A condition which could have been cured by adequate surgical drainage in from 30 to 60 days was prolonged for five months and during all of this time the patient was exposed to the calamity of the development of a chronic empyema.

Chronic Sterile Empyemas—Three patients developed chronic sterile empyemas while on penicillin therapy. In two instances, the complications were the direct results of delayed drainage of an empyema cavity containing thick sterile pus. The third case was complicated by a bronchopleural fistula. There is no question that penicillin therapy was of tremendous value in controlling a concomitant streptococcal pneumonia in this patient. The development of a chronic empyema was not influenced by chemotherapy.

SUMMARY—Our observations indicate that when suppurative pleuritis is caused by penicillin-vulnerable organisms, intrapleural injections of the drug will temporarily sterilize the pus. If the pus continues to thicken, however, it is usually necessary to perform surgical drainage to evacuate the material. If this is not done, a chronic empyema may develop and regardless of the sterility of the pus, the same problem of cavity obliteration remains to be solved.

As experience with penicillin therapy accumulates, the therapeutic approaches will become more standardized. Based upon our own observations, a tentative plan for the use of penicillin as an adjunct to the surgical treatment of acute empyema is suggested. 1. An injection of 50,000 units of penicillin may be given intrapleurally as soon as an infected fluid appears in the pleural cavity. It is important that treatment be withheld until the organism is positively identified. This precaution will prevent waste of penicillin in infections which do not respond to the drug, and an initial bacteriologic diagnosis will also rule out the possibility of a tuberculous effusion or empyema. 2. If systemic penicillin has been employed during the pneumonic stage of the disease, we believe it should be combined with local therapy. It is admitted that in many instances the pneumonic phase will have subsided by the time an empyema becomes apparent. The advantage of the systemic route, however, is that the blood will contain an antibacterial inhibitory substance which may control spreading cellulitis or invasive infection. It is our opinion, therefore, that systemic administration of penicillin should always be combined with local therapy. This is particularly true in cases of streptococcal and staphylococcal empyemas. Probably three intrapleural injections of 50,000 units on alternate days is sufficient for local treatment. Before the penicillin is injected into the pleura, as much of the infected fluid as possible should be removed by thoracentesis. If the pus continues to form and thickens, surgical drainage should be established. Temporary or even permanent sterilization of the pus does not alter the most important fundamental surgical principle in treating empyema thoracis, namely, adequate drainage.

PENICILLIN IN THE TREATMENT OF CHRONIC EMPYEMA

Systemic Administration—After adequate drainage of a chronic empyema cavity has been established, it appears that neither the local nor systemic administration of penicillin is important. During the period of observation to determine whether the cavity will become obliterated without further surgical intervention, there is little danger of spreading cellulitis or invasive infection. Continued fever and failure to gain weight and other manifestations of sepsis usually mean an undrained or inadequately drained collection of pus. No chemotherapeutic agent can be depended upon to replace proper drainage when dealing with pyogenic abscesses.

Local Penicillin—Until penicillin becomes as plentiful, and as inexpensive as Dakin's solution, azochloramid or even physiologic saline, its use as an

irrigating agent in drained abscess cavities will not be practical. Frequent irrigations with penicillin may eliminate from cultures penicillin-vulnerable organisms, but other common bacteria will persist. In five cases, daily irrigations of 25,000 units of penicillin were given for a period of ten days. In another six cases, both local and systemic penicillin were employed. Control cases with similar infections and approximately the same-sized empyema cavities were irrigated with Dakin's solution, azochloramid and saline. There were no significant differences in the time required for healing, and cultures from the cavities revealed a similar variety of organisms in all cases. The prevailing organisms were *B. proteus*, *B. aerogenes*, sometimes *staphylococcus*, occasionally *Streptococcus faecalis* and nonhemolytic *Streptococcus*. Cultures on different days revealed different bacteriologic patterns.

There are many disadvantages when penicillin is used for irrigations. To be effectual at all the agent must remain in contact with the tissues for some time. It is necessary, therefore, for the patient to remain in bed in the same position for several hours, so that the fluid will not be lost from the cavity. Irrigations at frequent intervals are precluded because of the extravagant amounts of penicillin which would be necessary.

Our experiences suggest strongly that the principal benefits of irrigations result from the mechanical cleansing of the cavity and not from any chemical or specific antibacterial effect of the irrigating agent.

Probably the most valuable rôle of penicillin in the treatment of chronic empyema is the protection which it may afford against spreading infection when a radical operation is undertaken for the obliteration of a chronic empyema cavity. When it is used as a prophylactic agent for this purpose, it is impossible to make a precise evaluation of its benefits. It seems reasonable, however, that when one is working through an infected or potentially infected field, penicillin protection may often prevent serious wound infections and other complications.

PENICILLIN AS A PROPHYLACTIC AGENT FOR THE PREVENTION OF POSTOPERATIVE EMPYEMA IN CASES OF LUNG RESECTION

Since postoperative empyema is the principal cause of both mortality and morbidity after resection of lung tissue, it is reasonable to utilize penicillin in an effort to reduce the incidence of this serious complication. When the mold first became available in limited quantities, we employed it in cases of empyema following pulmonary resection and were disappointed with the results. Penicillin was given both systemically and locally, and there was no positive evidence in six cases so treated that it had an appreciable effect upon the infection.

Recently, we have had an opportunity to utilize penicillin as a prophylactic agent in patients subjected to lobectomy for suppurative diseases of the lungs. Before enumerating our results it is important to consider a portion of White's⁴ report on a carefully performed clinical research project on the

same subject This study was under the supervision of Lockwood and Rhoads in connection with the activities of the Committee on National Research of the Office of Scientific Research and Development They found that penicillin was of greatest value in cases of suppurative pulmonary infections In 21 patients who had partial or total lung resection for bronchiectasis or multiple lung abscesses, ten cases subjected to lobectomy and two cases treated by pneumonectomy were given prophylactic injections of penicillin Penicillin therapy was begun seven days before the operation and continued for two weeks postoperatively in doses of 150,000 units daily Penicillin was not applied directly into the pleural space at the time of operation The control group consisted of seven lobectomy cases and two patients upon whom pneumonectomies were performed None of the patients receiving penicillin developed evidence of intrapleural infection All of the control group developed empyemas and three of them died as a result of infection

Our studies on the value of penicillin as a prophylactic agent in the prevention of empyema following pulmonary resection for suppurative disease of the lung are not strictly comparable to those reported by White Penicillin was started at varying intervals before the operations, and all cases receiving prophylactic intramuscular injections of penicillin also had 25,000 to 50,000 units of the agent placed in the wound at the time of operation The cases were not as carefully grouped as in White's studies, but the variety of lesions are approximately the same in the treated and in the control series

Thirteen of the patients in the treated group received penicillin the day of operation Seven patients received intramuscular injections 24 hours before the operation In two cases penicillin was given for three days before surgical intervention, for five days in two other cases, and for seven days in three others Two patients had been on penicillin treatment for three weeks before lobectomy was performed In all instances the dosage was 25,000 units intramuscularly at three hour intervals Penicillin was continued after the operation until the temperature was normal and the remaining lung tissue was fully reexpanded and the wound solidly healed

The length of time penicillin was employed preoperatively did not appear to influence the development of postoperative empyemas For example, the two patients who received the drug for three weeks before operation developed empyemas Both had pulmonary resections for chronic lung abscesses The incidence of empyema in cases treated from three to five days preoperatively was approximately the same as the patients started on penicillin protection 24 hours before surgical intervention

Summaries of the results in the treated group and in the control group are shown in Tables IV and V

It is apparent that the incidence of empyema is approximately the same in the two groups There was one death in the series of 59 cases which possibly could have been avoided if penicillin had been available It is interesting to note that in all patients subjected to pulmonary resection for

PENICILLIN IN EMPYEMA

TABLE IV
PENICILLIN-PROTECTED—PULMONARY RESECTION

Lesion		Empyema	Escaped Empyema
Lung abscess	2	2	0
Cystic disease	6	4	2
Bronchiectasis	21	5	16
	—	—	—
	29	11	18

SUMMARY OF THE INCIDENCE OF POSTOPERATIVE EMPYEMA FOLLOWING
PULMONARY RESECTION IN CASES WHICH HAD RECEIVED PENICILLIN
PROTECTION

TABLE V
CONTROLS—PULMONARY RESECTION

Lesion		Empyema	Escaped Empyema
Lung abscess	3	3	0
Cystic disease	7	3 (one death)	4
Bronchiectasis	19	6	13
Coccidioidal cyst	1	0	1
	—	—	—
	30	12	18

RESULTS IN 30 CASES OF PULMONARY RESECTION WHICH DID NOT HAVE
THE BENEFITS OF PENICILLIN THERAPY

chronic lung abscess a complicating empyema developed. However, empyema was avoided in a rather large percentage of cases operated upon for bronchiectasis. This finding corresponds with our experiences when the sulfonamides were employed in an effort to prevent postoperative empyemas and was true even before chemotherapeutic agents were available for this purpose. It is our impression that in our series of cases the incidence of empyema depended entirely upon successful closure of the bronchus. If the bronchus opened early during the postoperative course, a serious empyema developed. If it did not, empyema was avoided, or if it did develop after the remaining lung had reexpanded it was not serious. The only other justifiable conclusion from this study is that penicillin does not guarantee absolute protection from postoperative empyema in cases subjected to lung resection.

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- ⁴ Committee on Medical Research of the Office of Scientific Research and Development. Infected Wounds and Burns. Report No 35, September 8, 1944

DISCUSSION—COL I MIMS GAGLE, Atlanta, Ga. The edited transcript was not received in time for publication. If it is received before the "Transactions of the Southern Surgical Association" is published, it will appear therein.

DR FRANK K BOLAND, Atlanta, Ga. I should like to express my endorsement

of the remarks of the two previous speakers on penicillin as an adjunct. At the colored division of the Grady Hospital in Atlanta, Dr. Paul Beeson recently has treated 15 cases of acute empyema with injections of penicillin into the abscess cavity, and apparently has cured ten cases without surgical operation. Eight of these followed pneumococcal pneumonia, and two were the result of stab wounds of the chest in which streptococci were found. The success of the treatment seemed to depend largely upon whether or not accessory pus pockets were present.

After aspirating the cavity as free of pus as possible, from 12,500 to 20,000 units of penicillin were injected daily, or every other day, as cultures showed diminished infection. The treatment was necessary for from two to seven weeks before the discharge and fever disappeared. In cases that were operated upon, penicillin was continued as adjunct treatment. We have had no experience in treating chronic cases, but all surgeons must welcome the addition of any agent which will cure or help cure intractable chronic empyema.

At the present time penicillin is achieving remarkable results in medicine and surgery, but one or two years is not long enough to appraise its permanent therapeutic value. We should be slow to adopt exclusively any method of treatment as a substitute for good surgery.

DR. JOHN S. LOCKWOOD, New Haven, Conn. I think Doctor Blades is to be congratulated on having prepared this report based on experience in army hospitals, because it is to the army hospitals we must look for experience right now.

Our experience in the use of penicillin in treatment of pneumococcal empyema has tended to support the fact that where the organism is susceptible, repeated local injections of 20,000 to 40,000 units of penicillin associated with drainage or aspiration every day, or every other day, will often result in healing of the process, but I would be the last person to advise blind adherence to any form of chemotherapy in empyema. Each case has to be followed as an individual problem. If on the basis of roentgenologic and clinical findings the cavity is collapsing, then one is justified in proceeding with this course of treatment, but if there is evidence that the cavity cannot be evacuated by aspiration, or if the course is not proceeding satisfactorily, one should do thoracotomy and drainage. Penicillin is a help, but is certainly not the whole story, and it would be foolish to pretend that chemotherapy will be the answer in all cases. In multiloculated cases local therapy is not likely to succeed for obvious reasons.

In the failure of penicillin to prevent complications of lobectomy, I am frankly disappointed by Doctor Blades' experience. Our experience in Philadelphia certainly seemed to suggest that the systemic use of penicillin was a real milestone in prevention of complications. It seemed to have no value in tuberculosis or lung carcinoma, but in operations for bronchiectasis and lung abscess it seemed to be of distinct benefit. I do not know how to account for this contrast to Doctor Blades' experience. It may be because the patients in the Philadelphia group always received 150,000 units a day for seven days prior to operation. On the other hand, the favorable results may have been due to the fact that the series was comparatively small. In Doctor White's series there were only ten control cases, and 12 that received penicillin. This is too few to be certain of the statistical significance of the results.

I think it pertinent to point out that empyema which usually follows pneumectomy or lobectomy is usually a polymicrobial process. Many types of organisms may be present, some of which are resistant and some susceptible. As a rule, it is necessary to resort to the usual surgical methods in dealing with these infections once they become established.

Finally, I do believe it worth while to use penicillin in preparing patients with suppurative disease of the lung for operation. I recall one 14-year-old girl, ill for five months, running a septic temperature, and 120 cc of sputum per day, anemic—no fit subject for operative procedure. She was given penicillin, and within three or four days the temperature was normal and the output of sputum was down to 3 or 4 cc a day, even with postural drainage. There is no question that she was a better subject for lobectomy than before penicillin was administered. This is not a constant result, but even if only occasional, it is worth while to use penicillin in preparation of patients for surgery, and I believe we can increase the operability of patients with bronchiectasis. When it comes to abscess, with anaerobic bacilli, the results are not so satisfactory, and I do not believe

there is any panacea for treatment of chronic lung abscess, though here again, pre-operative preparation with penicillin is rational and should be used

I would like to close on the note that this is a subject on which there is tremendous need for further investigation. Nobody can offer any dogmatic statement concerning the possibilities of penicillin in pulmonary suppuration. There is ample evidence to warrant its use, but let us not get closed minds and develop any fixed opinion on any single type of treatment

DR J SHINGTON HORSLEY, Richmond, Va. In the ANNALS OF SURGERY, for September, 1944, Colonel Edward D. Churchill has an extremely interesting paper on the use of penicillin in the Mediterranean Area for which he is Consultant. This seems to have superseded to a large extent the various sulfa drugs

I would like to ask Colonel Blades about the methods of administration of penicillin. An article appeared in the November number of Science* in which the investigators showed that applying ice to the deltoid region an hour before the intramuscular injection, and for a few hours after the injection, delayed very materially the absorption of penicillin so that injections were necessary only about every five or six hours instead of every three or four hours

LT COL BRIAN BLADES, Washington, D. C. (closing) It is important to emphasize that the cases of acute empyema treated with penicillin had, in most instances, been treated elsewhere and referred to a thoracic surgery center after nonsurgical methods had failed. I have no doubt that a larger percentage of empyema cases treated by local penicillin may escape surgery than is indicated by our findings

Perhaps we were a little too radical in providing surgical drainage as soon as frank pus had formed. Our experience with chronic penicillin empyemas, however, made us feel that drainage should be provided if a true abscess of the pleura develops regardless of the temporary sterility of the pus

There is another factor which makes it difficult to evaluate the results with local penicillin therapy and repeated aspirations, namely, it is impossible to be sure when the empyema is really healed. One cannot measure the cavity and reliance must be placed upon roentgenologic findings. Since a rather large collection of fluid can be present in the chest and not be detected by roentgenologic examination, there is always some danger of a chronic empyema developing in cases thought to be cured by aspiration

Another important point to be considered is the danger of surgical drainage as compared with the danger of repeated aspirations. The so-called nonsurgical methods are not without danger. For example, in two of the patients in our series penicillin was injected into the lung tissue by mistake during the course of local penicillin and aspiration therapy. It seems reasonable to conclude that if aspiration treatment is carried to the fanatical extremes of 12 or 15 aspirations there will be about an equal chance of surgical accidents as when surgical drainage is carried out for a mature walled-off abscess

I should like to emphasize that we do not mean to imply that penicillin is not of value as an adjunct to surgery in lobectomy cases. Although, on a statistical basis, our series shows practically no difference, we have no intention of discontinuing the use of penicillin. We feel that the only conclusion to be drawn from our limited experience is that the mold does not afford absolute protection against postoperative empyemas complicating pulmonary resection cases

In all our cases penicillin was given by the intramuscular route at three-hour intervals. We have had no experience in the method mentioned by Doctor Horsley, namely, chilling the tissues to effect a gradual absorption of the penicillin. In this connection Romansky's work at the Walter Reed General Hospital might be mentioned. He has found that the administration of penicillin in beeswax in peanut oil results in satisfactory blood levels which are maintained for from 3 to 24 hours, depending upon the amount of penicillin given in a single injection. It is our intention to employ this technic in some of our lobectomy cases

*Trumper, Max (Lt Comdr), and Hutter, A. M. (Lt Comdr) Prolonging Effective Penicillin Action. Science, 100, 432-434, November 10, 1944

TOTAL HYSTERECTOMY*

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WHILE HYSTERECTOMY is an operation of a specialized field, it is one which the general surgeon is frequently called upon to perform. Probably the majority of hysterectomies are carried out as part of general surgical practice. For years the procedure was by the supracervical technic, as it still is, in most instances, in the treatment of benign lesions. Many surgeons, however, believe that, when the uterus is removed, whether the lesion be malignant or benign it is better to extirpate the cervix with it. It is unnecessary to extensively review before this group the arguments in support of the operation as a routine, or to enumerate those raised against it. The subject has become somewhat controversial.

Briefly, it is stated by one school that total hysterectomy should always be performed as it eliminates chronic infectious processes harbored within the cervix and effectually removes the possibility of carcinoma developing in the retained stump. From recent morbidity and mortality figures it is obvious, however, that for the occasional operator, it is better to adhere to the less formidable procedure for routine panhysterectomy, unless one has acquired skill from performing the operation many times, is fraught with danger and carries a higher mortality than the operation in which the cervix is permitted to remain. However, in large clinics where surgeons have perfected a technic in carrying out the procedure, mortality and morbidity are as low as is the case with the less formidable procedure. Under such circumstances, routine panhysterectomy is justified.

In weighing the advantages of panhysterectomy, one must take into consideration the higher incidence of complicating postoperative hemorrhage, damage to the bladder and ureters, cystitis, infection, phlebitis and thrombosis.

There are but two possible benefits afforded the patient by having the cervix removed simultaneously with the body of the uterus. The first is that it circumvents the development of cancer, providing it is not already present, and, second, it removes completely such infectious and inflammatory processes localized in the cervix, the possible precursors of carcinoma yet to appear.

Ward has stated the incidence of cervical stump cancer to be as high as 69 per cent. Others report it to be under 1 per cent. The average incidence taken from the figures of 16 different authors who have recently reported on the subject is 2.69 per cent (Table I). It has been thought that cauterization of the cervix, conization, the Stuehmordt operation, etc., would tend to decrease the incidence of carcinoma, possibly completely eliminating it. However, many instances of stump cancer, after such treatment, have been cited.

* Read before the Fifty-sixth Annual Session, Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

TOTAL HYSTERECTOMY

TABLE I
INCIDENCE OF CANCER IN REMAINING CERVICAL STUMP*

Author	Incidence of Cancer of Stump Per Cent
Behney C A	2 15
	4 7
Faehndrich J	1 28
Gagey J	3 45
Healy Wm and Arneson A N	2 6
Hochman S S	1 14
Johnson C G and Tyrone C H	2 2
Kretzschmar, N R and Gardiner S	1 7
Laborde S and Roques A	2 9
Martziloff, K H —Johns Hopkins Hospital 1889 to 1917	0 8
Martziloff K H —Collected statistics for The Johns Hopkins Hospital up to 1927	1 7
Meigs J V	1 9
	<u>2 1</u>
	4 0
Scheffy L C	3 6
von Graff	4 1
Mayo Clinic	3 97
Ward	6 00
Richardson	2 3
Average	2 69%

* From Martziloff

von Graff reporting 37 cases of cancer developing in cervical stumps after partial hysterectomy even after the cervix had been cauterized at the time of the removal of the uterus

If, as a routine procedure, removal of the uterus *in toto*, notwithstanding these benefits, increases the morbidity and mortality to the extent that it offsets these things, desirable as they may be, then the operation proves to be ill advised, at least in the individual surgeon's hands. If the mortality of total hysterectomy is to be greater than that of supracervical hysterectomy plus that of cancer occurring in the cervical stump, obviously the operation should not be performed.

These are truisms which have been set forth so many times that, no doubt, it is a matter of supererogation to again mention them before such an audience. They are referred to merely in connection with the general text of the paper, the chief object of which is to refer to an operation utilized by the author and to report the writer's more recent experiences with it.

Many surgeons conclude that cancer appearing one year or more after operation should be considered as definite evidence that no lesion existed in the cervix at the time of the original subtotal hysterectomy. Others believe that cancer developing in the remaining stump within three years following the original hysterectomy should be considered as probably existent at the time of the first procedure.

There has been great confusion in reference to this subject. The matter is approached variously and statistical analyses are frequently unreliable. As Martziloff has pointed out "It is one thing to speak of the incidence of cancer of the cervical stump in relation to cervical cancer in general and quite

another to speak of the incidence of cervical cancer among cervixes left as residua following supravaginal hysterectomy "

In any event, the question of whether or not a total hysterectomy should be performed in the presence of a benign lesion is largely a matter of individualization. The operation should be carried out if a diseased cervix is present or there is a certain prospect of its becoming so, but only if the operation can be performed without undue risk. I cannot accept the opinion that total hysterectomy should never be carried out except in the presence of carcinoma. Neither can I agree with those who advocate total hysterectomy as a routine.

TABLE II
MORTALITY IN HYSTERECTOMY*

Author	Mortality Total Hysterectomy Per Cent	Per Cent Supravaginal Hysterectomy Per Cent
Amreich, I	6	1.6
Danforth W. C.	1934 0.66	0.28
	1941 0.66	0.8
Doederlein	5.5	
Dupertuis S. M. and Zollinger R.	2.8	1.7
Faehndrich J.	4.2	1.5
	6.25	4.5
Franz K.	3.7	1.6
Fullerton W. D. and Faulkner R. L.	4.1	4.2
Kelly-Cullen		5.5
		1+
Kroenig	5.8	
Masson J. C.	1.2	0.9
Meigs, J. V.	4.4	2.9
Miller, H. E. and Prejean O.	1.33	2.75
Pearse R. L.		1.7
Reade C. D. and Bell A. C.	3.3	2+
Rinaman J. C. and Sellers T. B.	9.6	2.8
Siddal R. S. and Mack H. C.	6.4	2.6
TeLinde, R. W.	0	0.15
Waldeyer L.	2.2	
Weibel	3.5	4.25
Weir W.	3.1	
Albrecht H.	3.6	1.9
Doederlein	4.9	4.9
Average	3.87%	Average 2.35%

* From Martzloff

I feel that the weight of surgical opinion is that the total operation is one always of election to be carried out only when it can be skillfully done and with the minimum of morbidity and mortality.

The subject of complete removal of the uterus has excited considerable interest in the past decade, as witnessed by the hundred or more papers published on the subject in that period. From time to time the technic of the operation has been improved. Farrar, Richardson, Masson, and others, have recently described excellent methods.

The average mortality of a large number of operations performed by 22 reporting surgeons was 2.35 per cent for the subtotal operation and 3.57 per cent for total hysterectomy (Table II). With these figures before us, we may be justifiably dubious of the alleged over-all advantages of total hysterectomy.

tomy If these average mortality figures are to be those of an individual surgeon, then his course is well defined, and that is to employ only the less formidable procedure

The operation which the author has employed was described in a recent communication and the results with the first series of patients operated on by the technic was discussed in that paper¹

With the last 200 consecutive total hysterectomies performed, the morbidity has been minimum The patient left the institution on an average of the thirteenth postoperative day Sixty per cent of the patients were discharged on the twelfth postoperative day All recovered

The conditions for which the operation was carried out were

Fibroids	147	72.77%
Carcinoma of fundus or cervix	26	12.87%
Endometriosis	11	5.44%
Carcinoma of ovary	3	1.48%
In conjunction with removal of ov. cysts	9	4.45%
In addition to abdominoperineal resection for carcinoma of the rectum	1	.49%
Mis pathologic processes	5	2.47%
	<hr/> 202	

CONCLUSIONS

It may be assumed that the incidence of true residual cervical stump cancer is about 2 per cent Therefore, if one can constantly keep one's mortality well under 2 per cent, with no increase in operative complications, then is one justified in carrying out the complete operation If one's mortality is consistently greater than that expressed by an average irreducible minimum plus the percentage incidence of cervical stump cancer, then one's course is clear enough, and the subtotal operation should be performed The question of what procedure to elect resolves itself into a matter of what one's consistent results are as expressed in morbidity and mortality experiences

DISCUSSION —DR E H RICHARDSON, Baltimore, Md I doubt very much if most of the members of this Association realize from the splendid manner in which Doctor Foss has presented his paper, that in the American Gynecological Society this subject is almost as controversial as that of disks seems to be here There is a sharp difference of opinion among leading gynecologists in the country regarding routine total hysterectomy for benign disease when the cervix is normal There is no controversy as to the desirability of routine total hysterectomy when the cervix is diseased, but with a normal cervix I can see no reason for the more radical operation, and I have not yet found in the literature a convincing argument that justifies it Moreover, I think it is dangerous teaching to present statistics on hysterectomies which convey the impression that total ablation of the uterus is a simple easy procedure that can be carried out by the average surgeon I have not time to expose the fallacy inherent in such statistics, nor to emphasize the fallacy pointed out by Doctor Foss regarding the percentage of stump cancers in relation to cancer of the cervix as a whole

I prefer to utilize my time in presenting a brief summary of what I consider to be the most valuable recent contribution to discovery of unsuspected cancer of the cervix Dr R W Telinde, in collaboration with Dr G A Galvin, recently published the surprising results of a most important study In the clinic, a routine biopsy was taken

¹ Foss, Harold L., and Babcock, J Reed Total Abdominal Hysterectomy Surg, Gynec and Obst, 76, 214-227, February, 1943

from the cervix of every patient in the operating room and from many in the Out-Patient Department, to see in what percentage of cases there could be found early, but definite, malignant changes, and within a period of less than two years they have discovered in 16 cases the early histologic changes in the epithelium which have been recognized for some years by certain competent pathologists as incipient cancer. These changes are perfectly characteristic and are easily recognized by anyone familiar with the histology of this area. In these 16 cases in which these early preinvasive changes took place in the epithelium, the uterus was totally removed in all, and in 15 of them later in the laboratory, they were able by studying multiple sections to demonstrate definite invasion by carcinoma.

Furthermore, in a series of 300 cases in which total hysterectomy had been performed for benign disease, in which carcinoma was not suspected, four cases of unmistakable carcinoma were found. We are going to hear a great deal about this work I am sure, because it will undoubtedly be quoted as the final and convincing argument in favor of routine total hysterectomy. But I cannot subscribe to this view, because in all of these 16 cases the cervixes were diseased, they had chronic cervicitis or chronic discharge or slight bleeding. I have no quarrel with those advocating routine total hysterectomy in these cases, because I do it myself.

In my private practice over a period of 34 years, I have seen only one case of carcinoma of the stump of the cervix subsequent to subtotal hysterectomy.

I am familiar with Doctor Foss' operation, which is somewhat similar to the operation I published in 1929, devised to meet the three main causes of trouble in performing total hysterectomy, namely, hemorrhage during operation and postoperatively, postoperative peritonitis, and damage done to the bladder or ureters resulting in later fistulae. I spent 18 months developing this operation with the gratifying result that up to the present time, in a consecutive series of something more than 200 total abdominal hysterectomies for benign pathology, I have not had any troublesome hemorrhage during operation, no postoperative hemorrhage, no urinary tract fistulae and no postoperative peritonitis. I am, therefore, quite satisfied with this operation. I do not like the application of a clamp across the vault of the vagina nor the use of the cautery. I prefer rather to see the entire vaginal cuff open, so that I can ligate all bleeding vessels prior to its closure, and I am meticulously careful to cleanse the vagina and cervix as thoroughly as possible prior to the celiotomy, which I do myself, in addition to routine surgical toilet by an assistant.

In conclusion, permit me to say that I cannot endorse the teaching that total hysterectomy is as simple as subtotal, and that I do not believe any convincing evidence has been presented to justify the routine removal of a normal cervix when subtotal hysterectomy is indicated for benign disease of the corpus.

DR EMIL NOVAK, Baltimore, Md. I believe that Doctor Foss has given us a very fair appraisal of this problem which, as Doctor Richardson says, has long been a bone of contention among gynecologists. Almost *a priori*, I believe that everyone would concede that, if it could be done as safely as subtotal hysterectomy, the total removal of the uterus would be the operation of choice. The cervix serves no function after removal of the uterus, and just as good a pelvic floor can be given if it is removed. Its retention carries with it not only the possibility of later cancer but also of troublesome leukorrhea, even if such procedures as cervical cauterization are carried out. From time to time I have felt obliged to enucleate a cervix which had been left in perhaps years before, because of chronic infection and at times slight bleeding which caused concern as to the possibility of cancerous change.

On the other hand, to argue that total hysterectomy is always as simple and safe as the subtotal method appears to me to be rather absurd. While often it is, one should not forget that the removal of a cervix which may lie deep in the pelvis and be firmly fixed, carries one into a definitely dangerous zone so far as the ureter and bladder are concerned. Marked obesity, an unusually deep pelvis, extensive adhesions which fix the uterus and cervix almost immovably in the pelvis, extensive endometriosis which welds the uterus or cervix solidly to the rectum—these are some of the conditions which will influence me in a certain number of cases to choose the subtotal method. To insist on doing the total operation in all cases is just as bad surgery as never to do it.

Individualization is wise here as in every other surgical procedure. In spite of this, the total operation is done in the great majority, at least 75 per cent, of all my own hysterectomies. The more frequently one does the total operation, the easier one finds it to perform, and it is to be preferred unless some definite contraindication is encountered. By the same token, the occasional operator will probably be wise to select the subtotal method more often than the total. Were the latter attempted as a routine by relatively inexperienced men, it is certain that mortality and morbidity rates would both be increased.

To sum up, the chief factors on which the decision between total and subtotal hysterectomy in the individual case should be based are (1) a conscientious self-appraisal by the surgeon as to his own capabilities, (2) the technical problems presented by the individual case, and (3) the condition of the cervix.

Finally, I may say that I am familiar with the work alluded to by Doctor Richardson on very early phases of cancer. The latter, however, may be found in cervixes which show little or no evidence of laceration, chronic cervicitis or erosion, lesions generally thought to predispose to cancer. This constitutes another good reason for total hysterectomy as the method of choice. As a matter of fact, many of the earliest cancers I have seen have been in cervixes which showed little or no evidence of gross clinical change.

DR CURTIS H TYRONE, New Orleans, La. The edited transcript was not received in time for publication. If it is received before the "Transactions of the Southern Surgical Association" is published, it will appear therein.

DR HAROLD L FOSS, Danville, Pa. (closing) Doctor Richardson's figures dealing with studies of the cervix are interesting and the findings reported parallel those that have been presented at numerous times by other investigators. Cervixes permitted to remain following the removal of the body of the uterus may become carcinomatous in a certain percentage of cases but possibly in not over one or two. For this reason, if operative mortality, as I found it in studying the reports of many writers, is to be about 3 per cent for panhysterectomy, obviously, as Doctor Richardson states, it is bad teaching to advocate the operation as a *routine*, whether the lesion of the fundus is benign or malignant. However, this was strongly advocated recently in a paper coming from one of our leading medical schools.

A panhysterectomy in a stout individual may become one of the most difficult operations performed within the abdomen, yet in some institutions these procedures are routinely turned over to residents. In one large teaching institution, recently a mortality as low as 1.5 per cent was reported where routine panhysterectomies were carried out, many of the operations being performed by assistants. However, nothing was said with reference to morbidity. Prolonged hospital residence with delayed healing, with vesicovaginal and ureterovaginal fistulae are not uncommon in this operation and yet the patient may recover.

Doctor Novak sums up completely my own conclusions as I have attempted to express them in the paper and that is, that panhysterectomy should be performed when indicated, probably in the majority of cases but, as Doctor Novak concludes, the operation should be performed only when it can be performed safely. I thoroughly agree with Doctor Tyrone that the term panhysterectomy is not a good one. It has crept into the nomenclature only to cause confusion. The terms "total" and "subtotal" are better English and are more accurate and descriptive.

SURGICAL PRINCIPLES UNDERLYING THE USE OF GRAFTS IN THE REPAIR OF PERIPHERAL NERVE INJURIES*

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WITHOUT QUESTION the most substantial contribution which was made to the surgery of peripheral nerve injuries from the material studied during World War I concerned diagnostic principles. The important work of Pollock, Coleman, Stookey, and others, established the criteria necessary to diagnose divided nerves by correct sensory and motor examinations and recovering lesions after repair. Those basic contributions which dealt with sensory overlap and supplementary movements of muscles have never been successfully challenged. In fact, other data added subsequently have corroborated their correctness and have only added diagnostic methods which demonstrate the same principles. In addition, the work of Huber, and his associates, during World War I established certain equally important experimental and microscopic facts concerning the degeneration and regeneration of nerve fibers.

Unfortunately, the results of surgical operations performed upon nerve injuries during the last war have been a total loss as a contribution to surgical progress in this field. Military records were incomplete and unsatisfactory to begin with, and then were lost within the bureaucracy of government, so that a study has never been possible. Thus, of course, is a great surgical tragedy because if there can ever be any justification for war it lies in the compilation of data from the enormous number of injuries, to the end that mankind may eventually be the beneficiary. It is this lack of surgical data concerning the results of various technics of nerve repair and types of suture material used during World War I which had led to the occupation of younger surgeons with technical matters almost to the exclusion of other lines of investigation in the present war.

There is an astonishing lack of agreement concerning the principles of the treatment of peripheral nerve injuries. There are some who teach that peripheral nerves will never regenerate even if the ends are sutured accurately together under the most favorable conditions, and there are some who believe that the ends of a divided nerve trunk will, in some mysterious and serpentine-like manner, seek each other out and of their own accord form a union. Then, there are some experimentalists, without practical surgical training, who have devised various types of collagen, arterial, venous, and metal cylinders into which the nerve ends are placed so that the down-growing axis cylinders may be guided to a union with the distal segment. The hope, entertained by many surgeons, that a peripheral nerve injury will recover spontaneously has resulted in unjustifiable delays which have made

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successful repair impossible. Finally, it has never been sufficiently appreciated that the effector mechanisms, particularly the myoneural junctions in the muscles, are the most important factors in obtaining good functional results after nerve suture.

In September of 1942, it became necessary for the Senior Consultant in Neurologic Surgery to the European Theater of Operations to formulate a policy for the treatment of peripheral nerve injuries which would be simple, could not possibly be all inclusive, and would perhaps keep the young surgeons far forward in the combat zone from doing too little or too much.

There are certain simple, surgical principles which have been gathered from civilian and military experience and from the experimental laboratory which apply to the repair of injured nerves. The first, and most important, is that the ends of the nerve trunk should be brought into accurate apposition by an end-to-end suture at the earliest possible moment following division. This is the ideal situation which must be approached as closely as possible in the presence of the many factors which seriously interfere with its attainment.

The enormity of the soft tissue damage to an extremity may divert attention from the divided peripheral nerve just as a craniocerebral injury may cause one to overlook an injury elsewhere to the body. Cleansing of the wound with soap and water, careful surgical excision of the wound and realignment of a fracture of the bones must receive primary consideration, but they must be undertaken with the full realization that a missed opportunity to repair a divided nerve trunk early will result in a loss of function which nullifies the most accurately healed bony fragments. Therefore, if it is at all possible, the nerve ends should be apposed and united, with the finest silk and the smallest needles obtainable, by an accurate end-to-end suture which passes through the epineurium of the nerve and not through its substance. If the wound heals by primary intention, the best possible conditions for regeneration of the nerve have been established. If suppuration occurs, the nerve ends are in apposition and retraction with enormous bulbous or fusiform neuromas upon the separated ends will not make their resection, with a considerable loss of nerve trunk, necessary.

If there has been a loss of nerve substance so great that the nerve ends cannot be approximated, or if there is a bone or joint injury which does not allow the adjacent joint to be moved so that the ends can be approximated, or if it is surgically inadvisable to change the anatomic course of the nerve trunk, then it is incumbent upon the surgeon to identify the ends of the central and distal segments and introduce a metallic suture so that later secondary repair may be facilitated.

The question of whether or not a soft tissue injury can be closed after surgical cleansing and excision is sometimes not easily answered. This, then, raises the question of the value of the introduction of the sulfonamide drugs into the wound and their oral administration to control the course and virulence of the infection. The sulfonamides, or penicillin, do not and cannot

replace meticulous cleansing of the wound and surgical débridement. From experimental work which has been carried out in our laboratory upon gunshot injuries to nerve trunks in animals and from the examination and surgical treatment of extensive soft-tissue wounds with nerve injuries received in combat during the North African campaign by British and American soldiers, we believe that the sulfonamides properly used have a definite place in the treatment of such wounds and that they do not affect the regeneration and repair of the divided nerve.

It was recommended to the Chief Surgeon of the European Theater, that a sulfathiazole water-soluble jelly be made available to front line medical officers so that they might introduce it into the depths and crevices of an extensive soft-tissue extremity wound immediately upon its receipt. Following surgical cleansing and accurate débridement, the additional use of the sulfonamide powders or jellies will, in our opinion, make it possible to suture the divided nerve with greater safety from the effects of a suppurating wound. From our experience with extensive soft-tissue wounds with fractures of the long bones in which the nerve was not sutured at the time of the first definite surgical treatment, or was ignored, it became evident that such a healed wound, even though primarily infected, could be reopened, the nerve could be sutured and the wound closed without lighting up latent bacteria, within a much shorter interval of time, providing the sulfonamides were used locally in the wound at the time of the secondary operation and the sulfonamide blood level was adequate. This insurance was doubled if the sulfonamides had been used also at the time of injury and surgical débridement.

This free use of the sulfonamide drugs does not mean that we favor their use in every soft-tissue wound because we, also, believe that up to six hours, at least, after the receipt of a wound, it can be mechanically cleansed and surgically excised, the nerve sutured, the wound closed and primary union obtained. It does mean, however, that as a result of extensive experimental work we believe that although the local use of the sulfonamides may be followed by thin, silvery adhesions about the nerve trunk, and particularly at the line of suture, there is no definite demonstrable histologic evidence of interference with nerve axon regeneration.

As a matter of fact, there is reason to believe that the bugbear of the deleterious effects of infection upon the regeneration of nerve fibers is not as great as the habits of thought have led us to state. We have evidence to show that regenerating nerve fibers are not as vulnerable to infection as has been supposed. This is probably due to the inherent protective function of the perineurium against infection. We have seen histologic evidence of normal regenerating axons in the presence of suppuration which has affected the epineurium and the surrounding muscles or tendons. If, however, infection attacks the nerve fascicles, that is, if it exists within the perineurium, regenerating nerve fibers have never been seen to penetrate the area of leukocytic infiltration. Practically, then, this means that unless infection of

the exposed nerve fascicles in the severed ends of the nerve trunks exists, infection of the nerve bed or inflammation of the epineurium will not interfere with the down-growth of neuraxons into the distal segment

We have also shown, for the first time, the damage which occurs to the nerve trunks, both above and below the site of injury, by the concussive effect of a gunshot wound even though the nerve trunk has not been anatomically interrupted. The myelin sheaths break down in a similar manner, but to a greater degree, than is seen following the sharp severance of a nerve. There is molecular decomposition of the myelin, with localized edema, a process best called necrobiotic, and entirely different from secondary, or wallerian, degeneration. This necrobiosis occurs under conditions which have one factor in common—the damage to the myelin sheaths in combination with apparent damage to the Schwann cells, with survival of the mesodermal endoneural elements. The damage to the Schwann cells seems to concern chiefly their proliferating decomposition activities. They are not destroyed in milder traumatic damage where axis cylinders are seen to survive the demyelination. They enter into action in later nerve fiber regeneration and remyelination, but fail to digest the myelin.

Preceding nerve fiber regeneration, stimulation of the mesodermal cells by the non-fatty myelin decomposition products is very clearly seen and leads, wherever the traumatic lesion has reached a certain severity, to a confusion of the original endoneural structure and, by necessity, to a bewildering and irregular overproduction of regenerating nerve fibers. A heteromorphous nerve structure results. At a period when the neurotization is already well advanced, the myelin detritus can still be seen between the endoneural tubes and fibers.

Degrees of structural damage in such contused nerves may be found. The nerve with the slightest damage may show very little axis cylinder degeneration and for this reason only a relatively short transient disturbance of function, whereas, in a severe contusion even without any visible macroscopic nerve lesion, a complete wallerian degeneration of some or all nerve branches in combination with the heteromorphous type of endoneural proliferation and neurotization will be accompanied by a clinical picture similar to that produced by section of a nerve.

Nerve contusion may interrupt the continuity of the perineurium of nerve fascicles. This leads to a herniation of regenerating nerve fibers into the epineurium and the formation of traumatic neuromas. Again, the primary endoneural fibroblastic proliferation through the perineural gap results in the



FIG. 1—Sciatic nerve of cat 30 days following an end to end suture. The thin spider like adhesions which follow the use of the sulfonamide powders introduced into the wound are illustrated.

sprouting of regenerating nerve fibers into the epineurium. These fibers are lost for the neurotization of the degenerating part of the nerve distal to the injury. These observations explain why some nerve contusions are followed by hardly any, or only limited, interruption of motor and sensory functions, whereas, in other cases contusion leads to complete paralysis and often only imperfect return of function.

A nerve trunk completely severed by a bullet differs greatly in its histologic aspects from a sharply sectioned nerve. The traumatic destruction is much more severe and extends centralward in the proximal segment not just a few millimeters but, very frequently, several centimeters. This same effect may be seen reaching just as far distally in the distal segment of the damaged



FIG 2—Photomicrograph of section of the distal segment of a nerve following end to end suture. Sulfadiazine was used locally in the wound. There is some thickening of the perineurium and subperineural edema. The latter is entirely inside the perineurium and does not penetrate between the regenerating nerve fibers. Regeneration was as good close to the edema as at a distance. (Bodian fuchsin stain, $\times 85$)

nerve. The effect on regeneration manifests itself in the heteromorphous type of organization and neurotization of the entire traumatized area.

The most difficult surgical problem, however, concerns the treatment of those nerve injuries in which there has been a loss of continuity in the nerve trunk so large as to preclude an end-to-end apposition under any circumstances. The use of various types of nerve grafts, the fixation of joints and the transplantation of tendons have been advocated in the treatment of these injuries, some of which are preventable if the correct surgical treatment is employed when the patient is first examined. There is resistance and opposition to the use of nerve grafts on the part of some surgeons who observed their use during the last War. It must be said, however, that grafts were

not used properly at that time, nor were the results of their use ever evaluated, so that this total opposition is unwarranted. As a matter of fact, the experimental work of Huber, and his associates, and our own recent animal investigations upon nerve grafts are of sufficient promise to make it mandatory that the problem be settled once and for all upon the many severe nerve injuries which are present in many Army general hospitals today.

Cable grafts, in which many strands of small nerves are used to unite the central and distal segments of a nerve trunk, we believe are doomed to failure because of the technical difficulties of suture, but also because regenerating nerve axons do not reach the distal segment over a tangle of small nerve trunks. The increased amount of epineurium and the scar tissue which develops between each nerve trunk constituting the cable greatly interfere with the regeneration of nerve fibers by increasing the mesodermal barriers in their pathway. Fixed grafts of any kind, regardless of the material or the method of fixation, are total experimental failures, and the 27 human cases in which Soviet surgeons have used such grafts are absolutely inconclusive clinically and histologically. The most favorable type of graft to use is either an autogenous or an homogenous nerve trunk of equal size to the di-

vided nerve. Such autogenous grafts are impossible to obtain except in those instances, for example, in which all of the nerves to an upper extremity except the radial have been severed with a large loss of nerve trunk substance. Under such circumstances, it is entirely justifiable to sacrifice the ulnar nerve as an autogenous graft into the median in an attempt to regain sensory and motor function in the first finger and thumb. It is the homogenous type of graft which is most applicable, particularly in Army general hospitals which are amputation as well as neurosurgical centers.

The use of nerve graft banks is in a state of development. They involve elaborate preparations for freezing, drying, dehydrating and cold storage which must be made practical. From our experimental corroboration of Huber's work and from two patients operated upon in civilian practice, we believe that fresh homogenous grafts equal in size to the injured nerve should be used to repair large continuity defects in nerve trunks. Depending

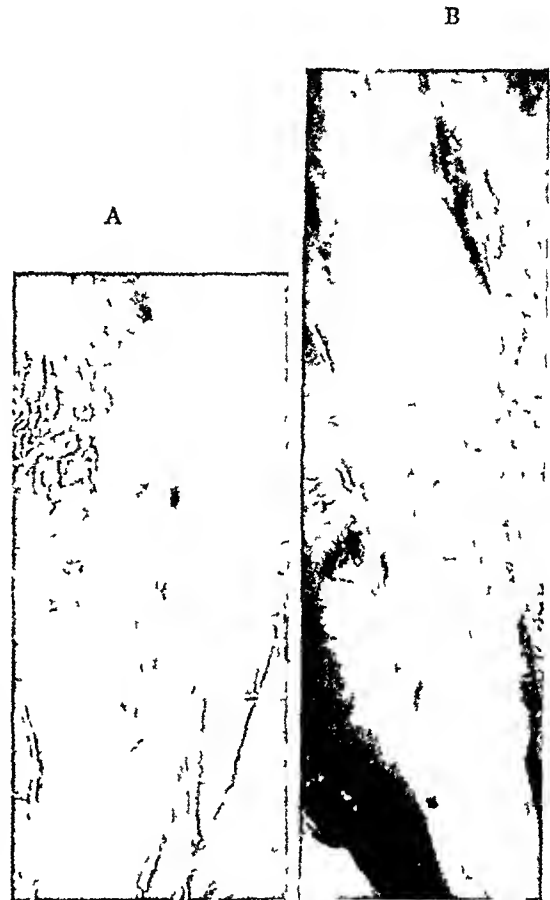


FIG. 3—(A) An autogenous graft 60 days after implantation, (B) an homogenous graft 60 days after implantation.

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upon the length of the graft, we believe that the distal suture line should be resected and resutured so that the down-growing axons in the graft can penetrate a less dense suture line into the distal segment. Animal experiments cannot provide complete proof of the practicability of this surgical step because the grafts used are not as long as those necessary in humans, but the evidence is in favor of such a procedure. It is quite possible that the dense

FIG 4

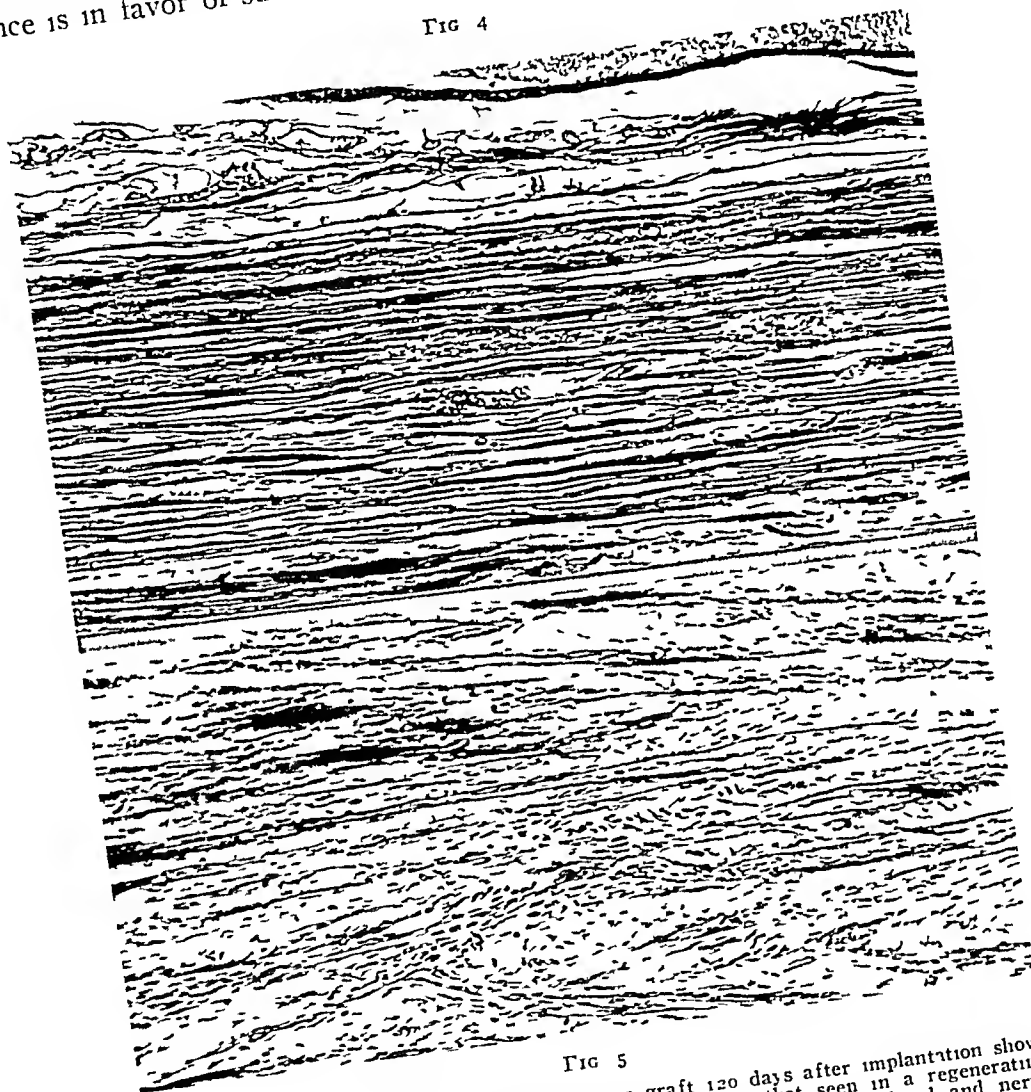


FIG 5

FIG 4—Photomicrograph of an autogenous graft 120 days after implantation showing an isomorphous structure and neurotization similar to that seen in a regenerating peripheral nerve. The old endoneurium is preserved and directs the band and nerve fiber proliferation. Remaining myelin decomposition products show an arrangement of original neurilemma tubes characteristic of a degenerating nerve. The borderline between perineurium and nerve fascicle is preserved. (Bodian fuchsin stain, $\times 190$)

FIG 5—Photomicrograph of an homogenous graft 52 days after transplantation showing an entirely heteromorphous structure and neurotization. Bundles of band fibers and regenerating nerve fibers pass between dense strands of proliferating collagenous fibers into the perineurium. (Bodian fuchsin stain, $\times 190$)

scar tissue which forms at the distal suture line in a long human nerve graft before the nerve fibers have been able to grow down that distance, prevents them from growing into the distal segment and may well explain the poor functional results thus far reported. Certainly the microscopic and clinical

FIG 6



FIG 7

FIG 6—Photomicrograph of the central segment of a nerve six days following a gunshot contusion. There is a destructive reaction of the axis cylinders some of which are swollen and disintegrated. There is a large amount of detritus and edema between the endoneurial sheaths. One nerve fiber shows a well preserved axis cylinder surrounded by a swollen and partly vacuolated myelin sheath. In other portions myelin sheaths are more or less completely destroyed. General cellular proliferation of the endoneurial cells and an accumulation of histiocytic elements within the detritus is seen. There is a beginning proliferation of Schwann cells. Nerve fiber regeneration is visible in the center. (Bodian fuchsin stain, $\times 450$)

FIG 7—Photomicrograph of distal segment of a nerve six days after gunshot contusion. The typical aspect of secondary degeneration is seen with the remainders of broken down axis cylinders, severely degenerated myelin sheaths with myelin globules small and large vacuoles and beginning cellular reaction. Comparison with Figure 6 shows the difference between a traumatic and a secondary degeneration. (Bodian fuchsin, $\times 450$)

evidence of two cases from civilian life would support such a step. The use of autologous plasma suture methods to unite the central and distal segments of the nerve to the graft should receive careful clinical and experimental evaluation. Theoretically, the absence of any tension should make this suture technic an ideal choice.



FIG. 8.—Photomicrograph of an infected end-to-end nerve suture after 14 days. Regenerating nerve fibers may be seen crossing the suture line and following the path of outgrowing fibroblasts and collagenous fibers. There is an abscess on the periphery (Bodian fuchsin stain, $\times 390$).

The distal suture line of a graft is always larger than the proximal suture line and it is larger in an homogenous graft than in an autogenous graft. It is the result of the endoneural and perineural mesodermal proliferation which unites the severed nerve ends to the graft. In our experiments homogenous grafts, even more than autogenous grafts, always appeared thicker at the time of removal than at the time of transplantation. This increase in size is closely related to the amount of proliferated mesodermal tissue within and around the graft and also to the structure of the graft itself. More and denser adhesions are present around the homogenous grafts because there is also a more pronounced perineural and epineural mesodermal proliferation, but these adhesions carry blood vessels to the epineurium of the graft, the nerve segment and to the suture line. The viability of the graft is wholly dependent upon its vascularization from the surrounding tissues and, therefore, any structure placed around the graft such as a tantalum or

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FIG 9



FIG 10

FIG 9—Photomicrograph shows an abscess within the epineurium and an intact nerve fascicle surrounded by intact perineurium in no way disturbed by the surrounding abscess (Bodian fuchsin, $\times 125$)

FIG 10—Photomicrograph of infected nerve suture showing degeneration with signs of trauma and beginning cell proliferation and inflammatory reaction. Connective tissue is seen growing at a right angle to the course of the nerve fibers. There is also proliferation of mesodermal tissue which seals off the endoneurial tubes of the central segment, and which grows from the perineurium into the gap between the central and distal segments (Bodian fuchsin, $\times 185$)

collagen cuff will prevent the growth of vessels into the graft and to that degree will interfere with the success of the transplant

Regenerating nerve fibers, preceded by Schwann cells, follow the path of proliferating histiocytes, be it in the granulation tissue that fills the gap between the central and distal segments at the suture line, in the proliferating endoneural sheaths of the degenerating distal nerve segment, the degenerated or necrotic graft, or wherever histiocytic proliferation takes place. Autogenous grafts are characterized by a predominantly isomorphous structure, that is one in which the original neurilemma structure is preserved. The majority of homogenous grafts show a heteromorphous structure, due to destruction of the original graft structure which follows the necrosis of the ectodermal and endoneural elements after transplantation. Neurotization of autogenous grafts is predominantly regular and parallel to the graft structure while in homogenous grafts the regenerating nerve fibers follow an irregular and deviating course. However, despite the large amount of regenerating nerve fibers lost in the epineurium of the suture lines and in the grafts of heteromorphous structure, the distal nerve segment often shows a satisfactory neurotization.

All operations for the repair of peripheral nerve injuries must be judged upon the basis of sound clinical examination for sensory and motor recovery, which appreciates the occurrence of overlap of sensation from adjacent uninjured nerves into the anatomic area of supply of the injured nerve and the development of supplementary muscle movements. In other words, recovery of function after nerve repair must be based upon the return of pin prick sensation in the isolated area of supply for pin prick of the injured nerve, and upon the patient's ability to perform muscular movements which are dependent upon muscles supplied only by the injured nerve. Strict adherence to these criteria will prevent reports of recovery of function after nerve repair which are either inaccurate or false.

Clinical and experimental observations warrant the statement that the operation of choice for the repair of an injured peripheral nerve in man, where direct end-to-end suture cannot be performed, is the transplantation of a nerve graft. The most satisfactory results can be expected from the use of a fresh autogenous graft of equal size to the injured nerve but if this is impossible to realize, the use of a fresh homogenous nerve transplant is justified. Finally, careful clinical studies before and after operation should be made upon the patients in whom such grafts are employed so that their value in man can be fully determined.

DISCUSSION —DR JOHN STAIGE DAVIS, Baltimore, Md. I would like to ask what is the greatest length of nerve graft Doctor Davis has been successful with.

LT COL MICHAEL E. DEBAKEY, Washington, D. C. I want to comment on one aspect of the subject referred to by Doctor Davis, that is the wasted knowledge concerning methods of treatment of peripheral nerve injuries in the last war. Recognizing the importance of this problem, the Surgeon-General has established a peripheral nerve injury registry for the purpose of evaluating the relative efficacy of different methods

of therapy as promptly as possible. It is believed that this procedure will provide valuable information long needed on the subject of peripheral nerve injury repair.

DR CLAUDE C. COLEMAN, Richmond, Va. I do not know of anything to disagree with in Doctor Davis' paper. I should like to say that Doctor Davis is one of the few men who kept up his interest in surgery of peripheral nerves between World War I and the present conflict. The lessons learned from the vast material of World War I in plastic surgery and other types of war surgery were subsequently applied in civilian practice, but peripheral nerve surgery received very little attention in the literature for two decades following World War I. As a result, it seems to me that these injuries have been very badly handled in civilian life. For instance, I think most of us have seen ulnar and median nerves sutured to the tendons at the wrist joint. This so-called "minor" operation of suturing nerves, after what is a very serious injury, should require the services of an expert surgeon and should not be entrusted to those not familiar with nerve surgery.

I want to emphasize one thing, that is, that out of the vast material of World War I we got practically no information insofar as the results of surgery were concerned. I was very actively engaged in nerve surgery of World War I, and I know nothing of what finally happened to these patients with nerve injuries. Occasionally, I examined one of the patients in Richmond but, as a whole, this vast material was not carefully studied for end-results. In this war, I think we all hope that there will be established criteria of recovery for every individual nerve. If we do this, and the cases are followed for three, four or five years after operation, we will then have the information we should have had following the last war. I am glad to know that steps have been taken to bring about a competent follow-up in nerve injury cases. We are in a different position in this war. We entered the war with a large number of surgeons trained in nerve surgery and we ought to get the maximum benefit from this experience.

There are certain inherent obstacles to complete success in nerve surgery. Some of these obstacles have been removed since World War I through better surgery and chemotherapy. At that time operations frequently had to be postponed because of persisting infection. This delay permitted the development of crippling sequelae from denervation, such as periarticular fibrosis and marked muscle atrophy. By supplementing adequate surgical treatment with chemotherapy, divided nerves can be repaired early, and early suture of peripheral nerves is always desirable.

DR JOSEPH E. J. KING, New York, N. Y. First, I want to thank Doctor Davis for this splendid paper, and in the same breath I would like to get after Doctor Coleman for his very modest attitude about the work he did during World War I, and should like to say of Doctor Frazier, and his staff, that the records were splendid and the work was good. All the books and monographs I have seen on nerve surgery contain no better sensory diagrams than those made by Baird, Buerki, Kennedy, Anderson, and others. The records they kept after suture, both in our department and in the physical therapy department, were complete in detail. That they may be buried under much bureaucratic dust I will agree, but that they were good I will assert. These records should be reviewed together with those found later in the Veterans' Bureau in order to learn about the results obtained.

I have been told by Foerster, Coleman, Frazier, and others (and it is my own experience and that of younger men today) that the best results to be expected from peripheral nerve surgery are in cases of accurate approximation of the ends with the least degree of rotation possible, without tension, and with good approximation of the ends with a very fine suture, and if the nerve suture is not done under these circumstances, a rather poor result can be expected. I have never heard of a perfect result in suture of a divided nerve. I doubt seriously that, if you divided a nerve and immediately resutured it, you would have a perfect recovery. However, we should attempt to attain good, if not perfect, results.

We were at a tremendous disadvantage in the last war in having patients come late after injury. Transportation was slow, the infected cases were many, and it took considerable time to clean up the infection. Therefore, our sutures were accomplished much later. Nevertheless, some good results followed nerve suture, even under these circumstances. I was consultant to the Veterans' Bureau for 15 years after the war.

and I saw a great many of these patients who had been operated upon by various men. Some of the results were pretty good, not perfect, but fairly good. I was able to follow up only five cases of nerve graft, and all I saw were failures. All were trellis-grafts placed in poor tissue—there was nothing else to be done—and all were failures. The subject of Doctor Davis' paper, the use of nerve transplants if they can be preserved and obtained from stock bottles, should offer some likelihood that good results may be obtained. But if trellis-grafts have to be used I think they will prove to be failures.

DR J ALBERT KLY, St Louis, Mo. I enjoyed this paper and am particularly interested that the fetish that the peripheral nerves are especially susceptible to infection has been quelled. It is my impression that they have stood up under infection very well. I think there is a marked tendency to put the bone lesion first, feeling that we must get the infection in the bone cleaned up before the nerve is sutured. This is a mistake. In some cases nerve suture should take precedence over the infection of bone. If the patient cannot use the hand it does not make much difference whether you get union or not.

I am glad to know that Doctor Davis has not thrown the sulfonamides out of the window. There is no question in my mind but that, if intelligently used, they will improve surgery. We cannot eliminate chronic infection in bone until we have excised it, but we can subdue it to a point where we can operate with impunity in the vicinity and avoid a late, usually futile nerve operation in dense scar tissue. Where you are going to transplant a nerve you can do the proximal suture first and let regeneration start, and suture the distal end of the graft to the distal end of the nerve at some later date.

COL E D CHURCHILL, Boston, Mass. Surgeons in an overseas theater are acutely aware of the difficult problem in peripheral nerve reconstruction that are being returned to the United States. I can only assure you that we have not been complacent about the matter, and many conferences have been held in an attempt to find a solution. At the present time the policy relating to the surgical management of anatomic severance of a nerve is as follows: (1) The forward surgeon at the time of the initial debridement makes a careful record of the injury as he observes it. Preoperative appraisal of nerve injury is notoriously difficult and meager in patients with multiple wounds, particularly if they are suffering from shock. The most precise information comes from anatomic observations at operation. Here again, it may not be desirable to embark upon a painstaking dissection with extension of the field of operation beyond the zone of devitalized tissues. (2) Dusting of the wound with sulfonamide may be omitted—certainly in the area of the nerve trunk. (3) Exposed nerves are covered with muscle so that the dry fine-mesh gauze used as a filler is not in contact with the nerve. Vaseline gauze is not recommended. (4) The joints above and below the point of injury are immobilized to minimize retraction of the nerve. (5) A firm pressure dressing supported by a plaster of paris shell is designed to reduce wound exudation. (6) Penicillin therapy is maintained by the systemic route. (7) On reaching a general hospital the original dressing is removed under aseptic precautions in the operating room. This usually is possible on or shortly after the fourth day after injury. The depths of the wound are revisioned and the nerve injury reassessed. Electrical tests may be made if desired. Oftentimes a more deliberate examination will correct or supplement the initial notes made in the forward area. Appraisal at this time is based on the ultimate functional restoration of the extremity, taking into consideration muscle damage and bone or joint lesions in relation to the nerve injury. Procedures such as muscle suture or even shortening of the limb by removal of devitalized comminuted bone fragments may be carried out at this time. The divided ends of the nerves may be approximated by a single fixation suture. The wound is closed if sepsis is not present, or if further excision of sequestering tissue adequately prepares the wound for closure. Closure of the skin may be further staged, or if a large skin defect exists, a skin graft is applied at once or as a staged procedure. (8) When first intention healing has been secured—and this results in 80 to 95 per cent of cases—formal suture of the nerve is undertaken. This should be feasible in many cases during the third or fourth week after injury.

Throughout the course of reparative surgery, the patient is protected from the hazards of invasive infection by systemic penicillin therapy. We do not consider that the local usage of sulfonamides contributes to the success of the program and, until

further evidence of its efficacy is presented, choose to use penicillin by the intramuscular route rather than as a topical application

During the staged operations of a program of reparative surgery, the red cell volume of the patient must be kept at normal levels by repeated whole blood transfusions

DR LOYAL DAVIS, Chicago, Ill (closing) As stated in my paper, I have had the opportunity in civilian practice of performing three nerve grafts, one autogenous and two homogenous grafts. In answer to Doctor Davis' question, the longest graft we have used measures five inches, and has been in place for eight years. All these grafts remained viable, and the most successful has been the autogenous graft, which we would expect from our experiments.

I am aware of the Surgeon-General's attempts to have patients with peripheral nerve lesions followed for a long period after repair. As a matter of fact, this was suggested in a memo written as Senior Consultant in Neurological Surgery in the European Theater of Operations, and I am delighted to learn that it has been put into effect, as Doctor DeBaakey has indicated. I think, however, it is necessary to go further and say that, when patients are discharged to the Veterans' Administration their compensation depends in part upon their willingness to return at designated intervals for examination by competent individuals.

As I have stated before, I had the opportunity of seeing soft-tissue wounds of the extremities complicated by peripheral nerve injuries among British and American soldiers in North Africa after they had been returned to England. All these wounds were weeks or months old and had not been closed primarily. The wounds had either suppurated or had been potentially infected, some had received sulfonamide at the time of injury some had not. The point I wish to make is that we were able to open those wounds, suture the nerve earlier, than we had ever dared in the past. Sulfonamides were used at the time the wounds were reopened and the wound sutured, but, inasmuch, as good surgical technique was also used it is not clear where the credit belongs. The point again, is that nerve injuries must be sutured early because atrophy of muscles, fibrosis of joints and tendons will occur to such an extent that even a nerve sutured end-to-end will not be successful because the end-organs, that is, the effector mechanism, cannot function.

We forget that a nerve will regenerate under the most unfavorable conditions, so that it is not a problem of regeneration of fibers so much as it is a problem of re-innervation of the muscles to which the nerve grows. It is the end-organ which is important. Splinting and massage help to keep the effective mechanisms in good condition, but without union of the nerve ends functional results cannot be obtained.

It is illogical and completely unsurgical to recommend a delayed peripheral nerve suture. This does not mean that under the terrific conditions of battle one must suture a nerve in an unsuitable environment, or under unsurgical conditions. It means only that those cases should be evacuated as rapidly as possible to a hospital and to a surgeon who is capable and has the facilities available for performing nerve repair. Any policy which does not make use of this fundamental process of joining nerve ends together at the earliest possible moment is surgically unsound. Delay also increases the neuroma formation upon the cut ends of divided nerve and results in a loss of nerve continuity. This may make it impossible to obtain an end-to-end suture, by any surgical procedure, which is the ideal method of repair. It may then become necessary to use nerve grafts and joint operations, which cannot hope to produce results that approach the return of innervation to the muscles supplied by the divided nerve.

As I stated, we are not among those who believe that the sulfonamides or any other chemotherapeutic agent should be used in all wounds. They will not replace surgical treatment. We have shown, however, that, in our opinion, their use does not interfere with the regeneration of nerve fibers. The policy of suturing peripheral nerves as early as possible has been justified, I understand, from the large number which were sutured within a few days after injury following the invasion of Normandy. If the young medical officers far forward are not sufficiently well acquainted with proper methods of treating soft-tissue wounds accompanied by peripheral nerve injuries, that is all the more reason why there should be a Consultant in Neurosurgery who is mobile enough to see these men and give advice, and help them with their problems.

OBSERVATIONS ON THE CONVERSION OF NORMAL INTO MALIGNANT CELLS*†

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THIS COMMUNICATION is an abbreviated account of some work carried out in the Tissue Culture Laboratories in the Johns Hopkins Hospital and the Carnegie Institution. A full and carefully prepared report is in preparation and will be published by Gey and Gey.

During the course of experiments requiring the continuous culture of rat mesenchyme, some of the normal cells became permanently altered. The characteristics of the altered cells led the observers to suspect that the cells had undergone malignant transformation. This alteration has occurred on three occasions. In two of these three instances the actual transformation was not observed at its inception, but on the third instance some of the earliest stages in the transformation were observed and recorded photographically.

The original tissue from which the cultures were started was obtained from a normal adult rat of the Philadelphia Albino strain. This strain has a very low incidence of tumors. A bit of subcutaneous areolar tissue was used for the primary explantation. Not all of the strains derived from this tissue have become altered; in fact, the oldest unaltered substrain is now over six years old and continues to reproduce with unerring accuracy cells that are morphologically the same.

The first alteration that occurred was noticed four months after the explantation of the subcutaneous areolar tissue. This deviation from the normal was the occurrence of many cells dividing in an abnormal manner. Not only did one see many tripolar mitotic figures, but also occasional tetrapolar ones. Over a period of weeks the proportion of abnormally dividing cells to normal ones steadily increased. Later changes in the size and shape of the cells and variations in the rate of cell division were observed. These changes gave rise to the suspicion that the cells had become malignant. To test this hypothesis, young healthy rats were inoculated with altered cells, and a very cellular sarcoma developed at the sites of the inoculations. These tumors were transplanted into other rats and produced invasive neoplasms which occasionally metastasized. Tissue cultures derived from these tumors usually grew rapidly. The cells in culture bore some resemblance to, but were not identical with, the altered cells which were first inoculated. In addition to the tumor derived from the initial inoculation, a number of other tumors were obtained by the

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periodic inoculation of subcultures of the altered cells. The cytologic appearance and behavior of these tumors differ widely from each other and from the original tumor.

The third instance of alteration of the rat fibroblasts occurred over two years after the explantation of the subcutaneous areolar tissue. This alteration when first seen in the living tissue culture consisted of the presence of rounded cells amid delicate sheets of fusiform fibroblasts. A liquefaction of the medium occurred whenever the rounded cells were present in large numbers. With prolonged cultivation the new cells increased rapidly in number, and abnormal mitoses were seen in these areas. A striking change took place in the nuclei of many cells. At first the newly altered cells showed nuclei that were slightly larger than those of the cells of origin. Later the nuclei became irregular in outline, very granular, and in stained preparations the altered nuclei were hyperchromatic. These changes, however, were not uniform, but in a single preparation one could see nuclei that varied greatly in form and size. Another evidence of alteration that became apparent was the change that occurred in the cohesion between the cells making up a colony. The normal fibroblasts produced colonies that showed rather marked cohesion, whereas the altered cells seemed to digest the surrounding medium and this resulted in loss of cohesion. Finally, the colonies of altered cells grew more rapidly than those of the parent strain. The changes just described were shown to be coincident with the development of malignant characteristics, for where colonies of altered and unaltered cells were inoculated into rats the former produced sarcomata at the site of inoculation, the latter never did so.

In every carefully planned experiment one always sets up adequate controls, but it is not possible to do so when the variables are still unknown. It is noteworthy, however, that some of the cells of the original explant have continued for six years to divide in an orderly manner and continue to produce cells that are morphologically and culturally identical with the original fibroblasts.

The possible explanations of the foregoing observations are several. Throughout the course of these experiments there were several strains of malignant cells being maintained in continuous culture in the laboratory. It might be conceivable that some of these malignant cells had contaminated the colonies of fibroblasts. That such contamination should occur three times with intervals of months, and always affect the subcultures of the same strain, is highly improbable. Furthermore, the appearance of the tumor cells of the altered strains is totally unlike any other cells seen in the laboratory. These differences in appearance were clearly brought out when mixed cultures of the existing malignant strains and the altered cells were prepared. Deliberate treatment of some of the normal rat fibroblasts with the cell-free filtrates of the culture medium maintaining other tumor strains growing in the laboratory did not evoke any permanent alteration in the fibroblasts.

It is well known that irradiation of normal tissue *in vivo* sometimes results in malignant transformation of the burned tissues. At the time of the occurrence of the first two alterations an experiment was being carried on in the laboratory to study the tolerance of certain cells to *gamma* irradiation. The radium was well shielded with lead, and the amount of stray radiation received by the cells was between 40 and 200 times the total natural earth radiation background. We know from other experiments in which several strains of normal rat fibroblasts were exposed continually to far greater doses of *gamma* rays that no permanent changes occurred. A stronger argument against the suggestion that stray *gamma* irradiation provoked the conversion of the normal into malignant ones is the fact that the third instance of this conversion took place several months after the experiment with radium terminated. Another agent capable of bringing about malignant changes in cells is one of the carcinogenic hydrocarbons such as methyl cholanthrene. During the occurrence of the alterations which form the subject of this communication there was no known contamination with any of the isolated carcinogenic compounds.

The medium in which the cells were grown was entirely heterologous except for a few passages at the time of the first explantation from the rat. In these few instances 10 per cent rat serum was added to the culture medium, but at all times thereafter the medium had the following composition: 10 per cent balanced salt solution, 10 per cent bovine embryo extract, 40 per cent human placental cord serum, and 40 per cent chicken plasma. It is true that such a medium is exceedingly rich in growth-stimulating hormones, but other strains of cells have been maintained in continual contact with media of this composition for over ten years and have not shown the transformation recorded in this paper.

Finally, a causative agent that might be suspected is the chance occurrence of a virus-like body. To test this hypothesis cell-free filtrates of the culture medium in which the alteration was occurring were added to the medium in which normal fibroblasts of the parent strain were growing but no mutation resulted. Similarly, cell-free filtrates of medium in which tumor cells had grown were used with negative results. These experiments, however, do not preclude the presence of a virus-like substance for it is possible that such an agent after entering or developing within a single cell might remain intracellular and be passed on to succeeding generations of cells at the time of division. Experiments are now in progress which were designed to test this possibility.

Among the many interesting speculations evoked by the observations recorded in this paper is one which we have attempted to study. The question arises what effect, if any, does a malignant cell have upon adjacent benign cells. A method has been devised by Doctor Gey for the isolation, without serious trauma, of a single malignant cell. Such cells have been transferred to culture media alongside normal fibroblasts. The division and subsequent multiplication of the malignant cell has been photographically recorded, and a tumor strain has been derived from such a single cell. In

the preliminary experiments, however, there was no discernible effect upon the fibroblasts

SUMMARY

A brief account is given of the transformation of seemingly normal rat fibroblasts into several strains of malignant cells. These conversions are permanent and are characterized by changes

- 1 In the morphology of the cells,
- 2 In the pattern of cellular division,
- 3 In cultural characteristics of the colonies

That these changes were evidences of the fibroblasts having become malignant was shown by the inoculation of altered cells into rats and the subsequent production of several different types of malignant tumors. Some possible explanations for the occurrence of these changes are considered, but the actual demonstration of a single causative factor is lacking.

DISCUSSION—DR J. SHELTON HORSLEY, Richmond, Va. This paper and demonstration is very interesting and thrilling. The cause of cancer with the changes between benign and malignant cells is a problem that has been studied in many laboratories. According to Ewing, the occurrence of cancer involves two factors. One is what he termed the *causal* genesis of cancer and has to do with the inciting factors leading to the development of malignancy. The other is the *formal* genesis which has to do with the factors responsible for the cancer cell and its unlimited capacity for growth. Many agents are involved in the causal genesis of cancer, but they may be considered as only starting a series of tissue changes or conditions which tend to turn into malignancy.

There are, of course, many things that seem to constitute either the causal genesis or the formal genesis for the conversion of normal cells into cancer cells. Aside from the carcinogenic chemicals and irradiation, estrogenic products and the milk factor are particularly interesting. It has been known for some years that in mice and even in rats cancer of the breast could be produced by giving excessive amounts of estrin products, and though this has not been definitely proved in humans, there are reported cases which strongly suggest that this sometimes happens in women.

In the milk factor which has been demonstrated quite clearly in mice, a newborn litter of mice from a high mammary cancer strain if nursed by a foster mother of low mammary cancer strain immediately after birth will develop cancer of the breast infrequently, following the attributes of the foster mother. Whereas, if a litter of mice from a low cancer strain is taken immediately after birth to a foster mother of high cancer strain, this litter will develop cancer of the breast in a high percentage of cases, behaving just as would a litter of the high cancer strain if nursed by the natural mother. Just what is the mechanism of this has not been definitely determined. It may be that all carcinogenic factors, as in the very beautiful culture experiments shown by Doctor Firor, tend to remove the inhibitory properties of the normal cells.

An observation of C. C. Little which appeared in the *Journal of the A. M. A.* of May 13, 1944, is an intriguing speculation. According to Little, the carcinogenic influences are not dependent upon stimulation of normal cells to new growth, but upon removal of inhibitory influences. The normal cell is kept in its place by some influences that control it, but the carcinogenic influence removes these inhibitions and the cell then reverts to its original primeval type, somewhat like the amoeba, and grows without any restraints. In other words, the carcinogenic agents act by removing the restraints acquired during the process of evolution and civilization of the cells, and they then run wild as they would without these inhibitions—this constitutes malignancy.

DR ALFRED BLALOCK, Baltimore, Md. Doctor Firor with his usual modesty claims very little credit for this work. Without attempting to discuss the interesting findings which have been related, I would simply like to say that Doctor Firor is in charge of the Division of Cellular Pathology in the Department of Surgery at Hopkins, and the staff, as well as the medical students, receive a great deal of benefit from following the important and fundamental work which is being performed.

MUCOID DISEASE OF THE APPENDIX^{*}

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AS THE VESTIGIAL REMAINS of an ancestral colon and of similar structure the vermiform appendix, with the notable exception of primary malignancy, is subject to the common diseases of the colon. The nature and the course of disease, however, are affected by the size, shape and position of the appendix, by the blood supply which is terminal, and by stasis which is a natural state. Chronic obstruction of the lumen with retention of its contents produces morbid changes in the anatomy and in the physiology of the appendix which, with their complications, are known as mucoid disease. Because of its chronicity and comparative rarity this condition has not received the attention that it merits.

In the stomach mucus is a protective mechanism, in the colon it is an agent for the lubrication of feces that become solid from loss of water by absorption. In both the colon and the appendix mucus is secreted by columnar cells lining simple tubular glands in the mucosa. Spastic colon,¹⁸ so-called mucous colitis, is a disease caused by a disturbance of the vegetative or autonomic nervous system that is marked by hypersecretion of mucus and by the passage of mucous casts of the colon. In it there are no symptoms referable to the appendix and it has no etiologic relationship to mucoid disease, although both the appendix and the colon are under autonomic nerve influence.

Chronic obliterative fibrosis from long-continued low grade inflammation converts the appendix throughout its length into a fibrous cord with loss of gland and of muscle structure. Chronic localized obstruction from stenosis, however, if of sufficient degree, is followed by cystic distention of the distal lumen. For distention to occur, secretion into the lumen must exceed fluid loss from it by drainage and by absorption. If enlargement is slow the resulting mucocoele or hydrops may ultimately approach the size of the gravid uterus at full term^{8, 9, 12, 21}. Rapid growth precipitates rupture. Fortunately, under modern conditions, most cases of chronic obstruction are operated upon as appendicitis before cystic change has become apparent. Increasing intraluminal pressure causes thinning of the appendiceal wall with the formation of diverticula. Diverticula occurring in the antemesenteric portion of the wall tend to rupture early, those developing into the meso-appendix grow more slowly and may themselves become secondary mucocoeles. Bailey,¹⁷ before this Association, has reported a case of a massive mucoid cyst of the meso-appendix, missed at appendectomy, being removed at subsequent operation. Mucocoeles produce indefinite symptoms and preoperative diagnosis is difficult.

Atrophy of the glands from intraluminal pressure may result in reduction of secretion into a mucocoele. Growth stops when fluid loss by absorption

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balances fluid gain from secretion. Continued secretion into a mucocoele with loss of fluid content by absorption results in the deposit of mineral salts as granules on the mucosa (Case 2) or as calculi (Case 4) in the lumen.



FIG 1.—Photograph of the appendix opened. Giant faceted calculus of the appendix.

Ogilvie⁷ has reported a case of 'cyst of the appendix, two and one-half by one and one-half inches in size, with calcification of the walls, in a railroad brakeman who complained of something solid "tapping him on the inside while he followed his daily work." Calculi may be multiple but as a rule are single. They vary in size, the largest reported¹⁴ was in a man aged 61, which weighed 13.5 Gm. It consisted mainly of calcium and magnesium phosphates. Mucocoeles rarely occur before middle age. We have seen, by invitation, a boy, age four, with a hard mass in the lower right abdomen which was shown roentgenographically to be a stone.¹³

The preoperative diagnosis was verified at celiotomy. The stone weighing 33 Grams, was contained in a mucocoele that had recently perforated.

The viscid contents of a mucocoele, like the white bile of a cholecystic hydrops or the clear fluid of a gonorrheal hydrosalpinx is practically sterile, and septic peritonitis does not follow rupture of a mucocoele as it does perforation in acute appendicitis. The opaque material that escapes from a mucocoele is not absorbed from the peritoneal cavity but blocks the lymphatics and remains as a foreign body to accumulate and produce ascites or "jelly-



FIG 2.—Roentgenogram of pelvis of four year old boy showing stone in mucocoele of the appendix. Case of Dr. Adcock.

belly," a bizarre disease that is termed pseudomyxoma peritonei. Due to chronic obstruction and inflammation the secretion into a mucocoele becomes changed from mucin to pseudomucin by metaplasia rather than by degeneration of the goblet cells. The great increase in the volume of pseudomucin that accumulates in the abdomen after perforation of a mucocoele makes it certain that, although transplants may not occur, secreting cells do escape from the appendix to live and to function in the peritoneal cavity. It is not logical to assume that the foreign body serositis which follows perforation activates the endothelial cells of the peritoneum to secrete pseudomucin.

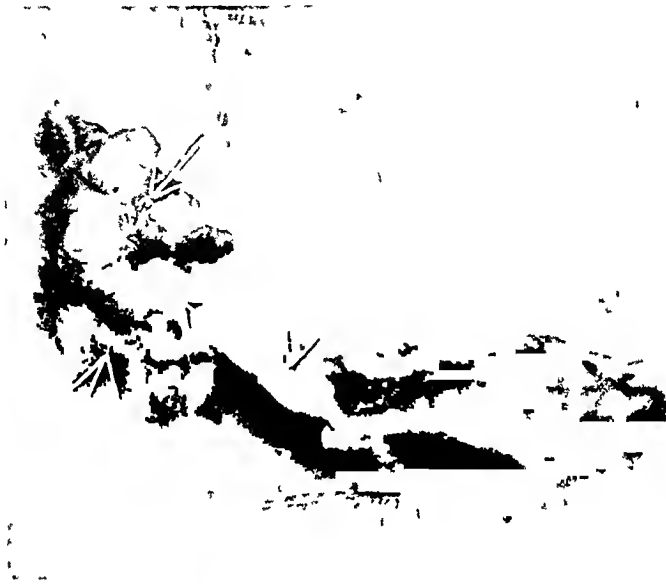


FIG 3—Photograph of mucocoele of the appendix opened, showing deposit of mineral salts on mucosa. Case 2

Largely because most cases of pseudomyxoma peritonei develop from rupture of adenomatous cysts of the ovary rather than from the appendix the disease is more common in women. It is not known why mucocoele of the appendix is found as an associated lesion in a high percentage of women who have developed pseudomyxoma peritonei from ovarian cystadenoma. In some cases the cystadenoma and the mucocoele have both ruptured and are found at operation to be discharging pseudomucin into the peritoneal cavity (Cases 3 and 4). Cystadenoma of the ovary is often malignant. Pseudomyxoma developing after the rupture of such a malignant cyst, although the cells are not invasive, is potentially carcinomatous, which terminates in death. Metastases from pseudomyxoma peritonei of ovarian origin have been found in the chest.¹¹

Woodruff and McDonald,¹⁵ reviewing 43,000 appendices removed at the Mayo Clinic, found dilatation in 146 cases, an incidence of 0.3 per cent. In ten of the appendices they found adenocarcinoma, and in four of the ten cases there was an associated malignancy of the ovary. They believe that fatal cases of pseudomyxoma peritonei which develop after rupture of

mucocèles all originate in carcinomatous cystadenomas of the appendix. Although they do not state that any of the 146 cases of mucocèle ruptured and developed fatal pseudomyxoma peritonei, their findings strongly suggest that peritoneal pseudomyxoma of *appendiceal as well as of ovarian origin* may be benign or malignant in type, depending upon the tissue from which it springs. Possibly cells originating in a benign lesion may assume malignant characteristics after they reach the peritoneum. Primary cancer of the appendix is rare, of low grade malignancy, and requires microscopic identification. Noiment¹ estimates that the relation of carcinoma of the appendix to carcinoma of other parts of the intestinal tract is as 1 to 250. I have never seen a case recognized by the surgeon at operation. Boyd²⁰ says true primary carcinoma of the appendix very rarely occurs. The condition commonly called primary carcinoma is really carcinoid tumor. It resembles carcinoma microscopically but is a benign lesion and is without symptoms.

Adenocarcinoma of the ovary is of frequent incidence and of high malignancy. Pseudomyxoma peritonei of appendiceal origin has a lower mortality rate. However, death in pseudomyxoma from either source may be mechanical and independent of cell structure, for it is most often due to intestinal obstruction. From serositis, pseudomucin in the free peritoneal cavity becomes enveloped into cystic masses of mucoid material which adhere to each other and to the viscera. Segments of small intestine may be bound in a colloid cast of the abdomen. Either condition results in chronic intestinal obstruction of varying degree. In late cases, that are operated upon after the intestine has become fixed, surgical treatment is futile.

Pseudomyxoma peritonei of appendiceal origin is a rare disease, less than 100 cases having been reported. The symptoms are those of a progressive, painless ascites which, untreated, results in death from intestinal obstruction. According to Seelig³ the disease may run a benign or a malignant course clinically without furnishing any differentiating criteria, macroscopically or microscopically.

Mucocèles of the appendix should be removed before rupture occurs and pseudomyxoma peritonei develops. After rupture, if the mucocèle, with all the pseudomucin that has escaped, is removed, the prognosis, in our experience, is good. Late cases, in which pseudomucin has become encysted and cannot be removed, tend to become obstructive. Drainage should not be employed. Cases that were drained by Ries⁵ to allow the escape of masses which could not be completely removed at operation all died. All cases should be reported in order that authoritative factual information may be obtained. At operation upon females there are often associated adenomatous cysts of the ovary which should be removed. In cases originating in carcinomatous lesions of either the appendix or the ovary, maximum dosage of deep roentgenotherapy should be administered postoperatively.

CASE REPORTS

Case 1—G. P. W., male, age 75, was seen July 2, 1937, with large bilateral inguinal herniae of long duration. At the repair of the right hernia, which was

strangulated, a perforated mucocoele of the appendix, the size of an adult thumb, was removed with 500 cc of brilliant amber jelly that was found free in the hernial sac and in the pelvis. Closure was without drainage. Radiation was not administered. On September 25, 1937, three months after dismissal, he returned for operation upon the left hernia, which had become strangulated. At this time the peritoneum was grossly normal and without pseudomucin or evidence of pseudomyxoma. He is reported to have died early in 1938 of hypertension.

Case 2—Mrs W R, age 58, giving the history of having had gallbladder trouble for 20 years, was seen April 11, 1941, suffering from acute cholecystitis, with stones. At operation, the gallbladder containing pus and faceted stones was removed. The uterus and the ovaries were atrophic. A mucocoele at the distal end of the appendix had ruptured, and about 750 cc of yellow colloid material was found free in the peritoneal cavity. This, with the appendix, was removed. The surface of the mucosa of the mucocoele was rough and granular like sandpaper from the deposit on it of mineral salts. The gallbladder region was drained. Recovery was without complication. No radiation therapy was administered. After three and one-half years she is in good health.

Case 3—Mrs W M S, age 61, has known she had had a slowly enlarging pelvic tumor for several years. She was suffering with abdominal pain of one week's duration. On examination, March 3, 1943, a cystic mass was found filling the pelvis and extending above the umbilicus. At operation, this proved to be a multilocular gelatinous cyst of the left ovary. Much yellow mucoid material from a ruptured loculus of it was free in the peritoneal cavity. There was a large mucocoele of the appendix with a small rupture through which jelly, similar to that coming from the ovary, was being discharged into the abdomen. After the peritoneum had been freed of pseudomucin, the left ovary, the appendix and the gallbladder, with stones, were removed. The wound was closed without drainage. The patient did not receive deep roentgenotherapy, and after 20 months is in good health. *Pathologic Diagnoses* (Dr Kenneth Lynch) Mucous cyst adenoma of the ovary. Mucocoele of the appendix. Pseudomyxoma peritonei. Cholecystitis, chronic, with cholelithiasis.

Case 4—Mrs J O, age 79, was admitted, March 3, 1944, complaining of difficulty in breathing and of progressive abdominal enlargement which began one year ago. Blood pressure and laboratory findings were normal. At operation, seven and one-half liters of thick yellow jelly were removed from the peritoneal cavity, much of it being contained in a massive papillomatous cyst of the right ovary that had ruptured. It was impossible to remove masses of jelly that were encysted in the great omentum and between coils of intestine. The left adnexa and the uterus were atrophic. There was a mucocoele of the appendix with a small perforation at the tip. The appendix and the right adnexa were removed. *Pathologic Findings* Cystic adenocarcinoma of the right ovary with rupture. Ruptured mucocoele of the appendix which contained a small calculus. Pseudomyxoma peritonei.

Convalescence was uneventful. Deep roentgenotherapy was administered. On examination, September 25, 1944, her condition was good, with no evidence of ascites.

COMMENT

We have reported two cases of pseudomyxoma peritonei of appendiceal origin, one in a man, age 75 (Case 1), the other in a woman, age 58 (Case 2). In both the condition was symptomless and was found incidentally at operation, in one for strangulated hernia and in the other for cholecystitis with stones. No pseudomucin was found in the abdomen of the man at a second operation performed three months subsequent to the first. We also report two cases (Cases 3 and 4) of pseudomyxoma peritonei in women, age 61 and 79, respectively, in both of whom there were mucocoeles of the appendix with small perforations. In both, the disease had apparently originated in

cysts of the ovary that had ruptured in one (Case 3), a benign cystadenoma, in the other (Case 4), an adenocarcinoma. In Case 4 the fact that the mucocele of the appendix complicating adenocarcinoma of the ovary was itself without gross or microscopic evidence of malignancy, proves that malignancy was not a factor in its development. In Case 2 there was a deposit of mineral salts on the mucosa, and in Case 4 there was a small calculus in the mucocele—so that all phases of mucoid disease of the appendix except the late obstructive stages of pseudomyxoma peritonei have been illustrated in the four cases. All the patients have been white.

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APPENDICITIS THE POSSIBLE EFFECTS OF SULFONAMIDES ON MORTALITY¹

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THIS REPORT constitutes a survey of 1151 consecutive patients with acute appendicitis who were operated upon at the Baltimore City Hospitals over a period extending from January, 1935, to May 1, 1944. Six hundred and fifty-one of these were operated upon prior to June 19, 1940, with a resulting mortality rate of 5.2 per cent, and 500 were operated upon since June 19, 1940, with a resulting mortality rate of 1.2 per cent.

In the beginning it should be emphasized that chemotherapy is not offered as a substitute for the fundamental rules that long have been practiced and recognized as most essential in the treatment of this disease. Early diagnosis and operation before the peritoneum has been materially soiled and careful handling of the intra- and extraperitoneal structures during operation are still most important factors in the control of this disease. It is also necessary to stress the fact that sulfanilamide is not administered either locally or systemically in those cases where the peritoneal cavity does not contain free pus, unless there develops some pulmonary or other complication. The available data on this subject, as well as the remarks made here, do not prove conclusively the value of the sulfonamides in this disease, whether they are used topically or otherwise.

It has been the practice in this clinic for many years, with few exceptions, to subject all patients suffering from acute appendicitis to an immediate operation. It is realized, of course, that the application of this rule in patients with far-advanced diffuse peritonitis is questionable. Many competent surgeons are of the opinion that a period of conservative treatment should be instituted before operation where such a condition exists. It is not the purpose of this paper to discuss the advisability or inadvisability of this rule. It is felt however, that in a municipal hospital where a house officer staff is maintained with a chief resident who has had an experience of only five or more years of graduate hospital service, and where many of these patients are treated by the house staff in conjunction with members of a visiting staff, it is necessary to adopt a rather dogmatic policy with regard to the handling of routine patients. Therefore, more or less definite rules are followed in the treatment of various diseases and the disease under discussion is no exception. This does not mean that these rules are hidebound and that exceptions may not be made, but, in the main, the following rules apply.

(1) All patients whose symptoms present the picture of acute appendicitis

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are subjected to an early operation. If necessary, supportive treatment is instituted prior to or during the operative procedure. (2) A McBurney incision is made in almost every instance where the preoperative diagnosis of acute appendicitis seems reasonably certain. Right rectus and midline incisions are made infrequently. (3) Black silk is used throughout in most instances of simple acute appendicitis. However, catgut is employed in potentially infected cases. Plain 0 or 00 chromic catgut is used for appendiceal ties and inversion of the stump is always carried out where the procedure is technically possible. The purse-string usually consists of double A oiled silk suture. (4) In patients with appendiceal abscess the appendix always is removed if it is readily accessible or if it can possibly be removed without breaking down the limiting abscess wall. (5) In more recent years sulfonamides have been used in the contaminated peritoneal cavity and systemic doses of the drug are given later. Prior to June, 1940 no sulfonamides were used consistently either in the peritoneal cavity or by oral methods.

In this review it is desired to point out the use and possible effect of the sulfonamide drugs on the mortality and, to a lesser extent, the morbidity rate. To suit the purpose of this discussion the usual pathologic classification, namely acute catarrhal, acute suppurative, acute perforative, and acute gangrenous appendicitis is being omitted. Instead the following classification is being made: simple acute, early perforative, appendiceal abscess, and perforation with diffuse peritonitis.

Outside of two anesthetic deaths which occurred on July 17, 1941, and October 5, 1941, respectively, there have been four deaths from acute appendicitis since June, 1940. This covers a period of almost four years, and gives a mortality rate, excluding the two anesthetic deaths, of 0.8 per cent against an over-all mortality rate of 1.2 per cent.

In this series of patients operated upon since July 19, 1940, and repeating again that the two anesthetic deaths referred to have been excluded, there were 27 patients with acute appendicitis and abscess formation, with one death. This is equivalent to a mortality rate of approximately 3.7 per cent.

There were 26 patients with acute appendicitis and early perforation and, again disregarding the one anesthetic death that occurred in this group, there were no deaths. There were 418 cases of simple acute appendicitis in which no sulfonamide drugs were used and there were no deaths. In addition, there were 29 patients with perforation and diffuse peritonitis, with three deaths. This gives a mortality rate in the latter group of approximately 10.4 per cent. The foregoing groups total 500 patients operated upon for acute appendicitis and, excluding two anesthetic deaths, gives a mortality rate of 0.8 per cent.

Prior to June 19, 1940, there were 56 patients treated for acute appendicitis who had early perforation. From this group there was one death, giving a mortality rate of approximately 1.8 per cent. There were 31 patients with abscess formation, and in this group there were three deaths, the mortality rate being 9.7 per cent. In addition, there were 87 cases diagnosed as acute

TABLE I
SUMMARY OF ALL DEATHS OCCURRING IN 1151 CASES OPERATED UPON FOR ACUTE APPENDICITIS

Classification of Disease										Perf with Diff				Sulfonamide Therapy				Drains		Anesthesia		Surgical Path		Remarks
Case	No	Race	Sex	Age	Hosp Days	Date of Death	Simple Acute	Early Perf	Pento-Peritis	Perf	with Diff	Perf	Perf	Perf	Perf	Perf	Perf	Perf	Perf	Perf	Perf	Perf	Perf	Perf
(1)	8179	W	M	35	1	7-17-35								No	No	No	No	Perito	Perito	Sp N	Sp N	Gang	Gang	Anesthetic death
(2)	9862	C	F	29	4	10-18-35								No	No	No	No							Patient died before incision was made Six-mo pregnancy Autopsy showed peritonitis with diffuse peritonitis
(3)	10026	W	F	65	2	10-22-35								No	No	No	No	Fascia	Fascia	Sp Pont	Sp Pont	Acute	Acute	Paralytic ileus Bronchopneumonia
(4)	10508	W	F	22	7	11-21-35								No	No	No	No	Perito	Perito	Sp Nov	Sp Nov	Acute	Acute	Postoperative ileus Patient was pregnant
(5)	11229	C	M	50	5	12-23-35								No	No	No	No	Perito	Perito	Sp Nov	Sp Nov	Perf	Perf	
(6)	12854	W	F	58	4	3-9-36								No	No	No	No	Fascia	Fascia	Sp Nov	Sp Nov	Acute	Acute	
(7)	14349	C	F	40	1	5-27-36								No	No	No	No	Perito	Perito	Sp Nov	Sp Nov	Acute	Acute	
(8)	14426	W	M	5	1	5-31-36								No	No	No	No	Perito	Perito	Gen	Gen	No rep	No rep	
(9)	14501	C	F	40	1	6-4-36								No	No	No	No	Perito	Perito	Sp Nov	Sp Nov	Gang	Gang	
(10)	14869	W	F	6	1	6-25-36								No	No	No	No	Perito	Perito	Gen	Gen	Acute	Acute	
(11)	15070	W	F	41	8	7-20-36								No	No	No	No	To peritoneum	To peritoneum	Sp Nov	Sp Nov			Appendix not removed Right tube and ovary gangrenous--removed Delivered full term child 48 hours before surgery Postoperative ileus and peritonitis Autopsy showed localized peritonitis atelectasis, stump intact
(12)	16665	W	M	64	2	8-27-36								No	No	No	No	Perito	Perito	Sp Nov	Sp Nov	Acute	Acute	Appendix was removed Postoperative peritonitis and cellulitis of abdominal wall Autopsy showed perforation of cecum
(13)	15673	W	M	57	12	9-28-36								No	No	No	No	Perito	Perito	Sp Nov	Sp Nov			Far advanced bilateral pulmonary tuberculosis Hemiplegia Postoperative bronchopneumonia Autopsy showed paralytic ileus, appendectomy and hysterectomy, localized hemorrhagic peritonitis, no perforation of stump definite
(14)	15441	W	F	32	10	11-30-36	1							No	No	No	No	No	No	Sp Nov	Sp Nov	No rep	No rep	Appendix removed Postoperative pneumonia and peritonitis Anesthetic death
(15)	20816	W	M	62	4	2-7-37								No	No	No	No	Perito	Perito	Gen	Gen	Acute	Acute	
(16)	20980	W	F	41	6	2-16-37								No	No	No	No	Under fascia	Under fascia	Sp Nov	Sp Nov	Acute	Acute	
(17)	23497	W	M	43	6	5-17-37								No	No	No	No	To cavity	To cavity	Sp Nov	Sp Nov	Acute	Acute	
(18)	24836	C	M	14	1	7-8-37								No	No	No	No			Gen	Gen	Perf	Perf	

(19)	27533	W	M	63	7	10-22-37	1	No	Perito	L Nov	Gang	Autopsy showed perf of stump with gen purulent peritonitis, lobular pneumonia, syphilitic aortitis, aortic and coronary sclerosis
(20)	27500	W	M	26	9	10-23-37	1	No	No	Sp Nov	Perf	For advanced bilateral pulmonary tuberculosis I and D of scrotal abscess 5 days postoperative with resultant staph septicemia (positive blood culture)
(21)	29047	C	F	54	20	1-2-38	1	No	Perito	Sp Pont	Perf	Autopsy showed diffuse peritonitis and perforation of terminal ileum Hysterectomy and bilateral salpingo-oophorectomy at time of operation also
(22)	31332	W	M	7	1	3-4-38	1	No	Perito	Gen	Perf	Patient moribund on admission
(23)	32019	W	F	20	7	4-4-38	1	No	Perito	Sp Nov	Perf	Postoperative bronchopneumonia, pelvic abscess with I and D
(24)	32549	W	M	57	1	4-16-38	1	No	Perito	Sp N & G	Acute	Subsequent operation for intestinal obstruction, postoperative pelvic abscess
(25)	34555	C	M	29	30	7-23-38	1	Prontosil	Perito	Sp Pont	Perf	Massive atelectasis
(26)	36298	W	M	18	1	8-21-38	1	No	Perito	Gen	Perf	Subhepatic abscess, gangrene of anterior abdominal wall
(27)	38621	W	F	50	10	11-22-38	1	No	No	Gen	Acute	Bronchopneumonia, paralytic ileus
(28)	41117	C	M	54	3	1-22-39	1	No	Perito	Sp N & G	Perf	Late diffuse peritonitis
(29)	42889	W	F	73	1	3-14-39	1	No	Perito	L Nov	Gang	Pulmonary embolus Sudden death
(30)	48220	W	F	55	3	9-13-39	1	No	Perito	Gen	Acute	
(31)	52323	C	M	52	3	1-30-40	1	No	Perito	L Nov G & O	Perf	
(32)	52514	W	M	50	9	2-10-40	1	No	Perito	Sp Pont	Gang	Bilateral advanced pulmonary tuberculosis
(33)	54349	C	F	43	4	4-7-40	1	No	No	Gen	Gang	
(34)	52981	W	M	45	77	5-5-40	1	No	Cavity	Sp Nov	Acute	Subsequent I & D of subhepatic and subdiaphragmatic abscesses, pulmonary embolism
(35)	56562	C	M	17	6	6-19-40	1	Sulfanilamide	Perito	Sp Pont	Perf	
(36)	59306	C	F	13	3	9-21-40	1	Sulfanilamide	Perito	Gen	Acute	Patient in <i>extramis</i> at time of operation
(37)	63922	W	M	17	3	2-27-41	1	Sulfanilamide	Perito	Sp Pont	Perf	Subsequent generalized peritonitis
(38)	67486	W	F	7	1	7-17-41	1	No	No	Gen	Acute	Anesthetic death Patient died as appendix was being amputated
(39)	69202	C	M	44	1	10-5-41	1	No	No	Sp Pont		Anesthetic death Appendix not removed
(40)	71032	C	M	59	3	1-12-42	1	Sulfanilamide & sulfathiazole	Perito	Gen	Gang	Paralytic ileus

appendicitis that had perforation with diffuse peritonitis. From this group there were 27 deaths, with a mortality rate of approximately 31 per cent.

A review of the records of the patients reported here shows that the sulfonamide drugs have been used in nearly all perforated appendices since June, 1940. It was then that the rule was made for the administration of sulfanilamide in patients with free pus in the peritoneal cavity. There were a few instances in which it was used before that time, but only spasmodically and with no regularity in regard to the type of peritonitis or the amount of the drug.

From these statistics one might conclude that the drug has probably been an important factor in lowering the mortality rate for diffuse peritonitis which has dropped from 31 to 19.4 per cent, and appendiceal abscess from 9.7 per cent to 3.7 per cent since its routine use. It should be borne in mind, however, that there are many factors that influence mortality and these figures should not be considered conclusive.

If these observations are significant the question arises as to the effect of the drug on the organisms causing the disease. Up to the present time that question cannot be answered satisfactorily. The chief difficulty is that the bacterial flora of the intestinal tract is not too well known nor is it constant. This is well illustrated in infancy by comparing the bacterial flora of the intestines of artificially fed and breast fed babies. The former show a richer colon and anaerobic spore-bearing group of organisms. In adult life the colon group constitutes approximately 75 per cent of the intestinal flora. Hertei,² Kendall³ and Rettger⁴ have done considerable research and have shown that the bacterial content of the bowel may be changed by adjusting the diet. Eggert,⁵ in 1935, described 11 species of gram-positive nonsporulating anaerobes isolated from the feces. It is thought that most of these organisms are nonpathogenic but it is also believed that some of them, under varied circumstances, may be or may become pathogenic. Whether these organisms normally present in the intestinal tract are the chief exciting factors in the causation of acute appendicitis is not known. Since the bacterial flora is altered by change in diet, acute appendicitis may be caused by some of the better known organisms that are influenced by the sulfonamide group of drugs. The sulfonamides may possibly have some inhibitory effect on the synergistic activity of two or more of the organisms in question, thereby, lessening the destructive activity formerly observed in localized or diffuse peritonitis.

The choice of sulfanilamide in preference to sulfathiazole for use in the general peritoneal cavity was made because of its greater absorptive power. One of the authors (T. B. A.) frequently has introduced from 4 to 10 Gm of sulfanilamide into the peritoneal cavity and found that the blood level was 6 to 8 mg per 100 cc the following day. It would seem, therefore, to hold preference in absorptive power over all of its allied drugs. This is apparently desirable because it is thought to have little or no effect locally, however, the systemic effect is probably responsible for whatever beneficial results may

SULFONAMIDES IN APPENDICITIS

TABLE II

PATIENTS TREATED WITH SULFONAMIDES

Early Perforation		Abscess Formation		Diffuse Peritonitis	
No. of patients	26	No. of patients	27	No. of patients	29
Deaths	0	Deaths	1	Deaths	3
Mortality rate	0%	Mortality rate	3.7%	Mortality rate	10.4%

TABLE III

PATIENTS TREATED WITHOUT SULFONAMIDES

Early Perforation		Abscess Formation		Diffuse Peritonitis	
No. of patients	56	No. of patients	31	No. of patients	87
Deaths	1	Deaths	3	Deaths	27
Mortality rate	1.8%	Mortality rate	9.7%	Mortality rate	31%

TABLE IV

AVERAGE DAYS IN HOSPITAL—WITH USE OF SULFONAMIDES

Early Perforation	Abscess Formation	Diffuse Peritonitis
13	28	23

TABLE V

AVERAGE DAYS IN HOSPITAL—WITHOUT USE OF SULFONAMIDES

Early Perforation	Abscess Formation	Diffuse Peritonitis
11	31	20

TABLE VI

MORTALITY ACCORDING TO AGE GROUPS

Years of Age	Number of Deaths
0-10 inclusive	4
11-20, inclusive	6
21-30 inclusive	4
31-40, inclusive	4
41-50 inclusive	9
51-60, inclusive	8
61-70 inclusive	4
71-80 inclusive	1

TABLE VII

TYPES OF ANESTHETIC USED

Spinal novocaine	450
Spinal pontocaine	342
General (G O E)	283
Spinal novocaine (supplemented by general or sodium pentothal)	26
Spinal pontocaine (supplemented by G O E or sodium pentothal)	22
Local novocaine (some supplemented with gas oxygen)	13
Sodium pentothal (with or without gas oxygen)	15
	<hr/> 1151

TABLE VIII

TOTAL PATHOLOGIC REPORTS¹

Perforated appendices	80
Gangrenous appendices	76
Acute appendicitis (including suppurative cases and some gangrenous and perforated cases)	533
Subacute appendices	175
Essentially normal appendices	143
	<hr/> 1007

¹In 144 of 1151 cases no pathologic reports are available

follow. The same conclusion is found in the work of Meleny, and his co-workers.⁶ In addition, sulfanilamide probably causes fewer intraperitoneal adhesions. This inference is based largely on the work of Boys and Lehman.⁷

The mortality rate has been reduced during the last four years in this series, and may have been influenced by the institution of sulfonamide therapy. It is not believed, however, that the rate of morbidity has been lowered to any appreciable degree. A study of Table IV will show that the average period of hospitalization has not been reduced as a result of the institution of the drug. The same observation has been made with regard to the extent of local infections.

The type of anesthesia ordinarily preferred was spinal pontocaine or novocaine. In this group of 1151 patients spinal anesthesia was employed in 840 cases and a supplement of nitrous oxide and oxygen or pentathol sodium was used in 48 instances. When spinal pontocaine was used it was mixed with 10 per cent glucose. Local novocaine, intravenous sodium pentathol, or general inhalation anesthesia was preferred in the patients who were considered in poor physical condition. This preference was expressed because of the reluctance to use spinal anesthesia in poor risks. Whenever an intrathecal injection is made a mixture of pituitin and ephedrine is available to give before or during the period of anesthesia.

As mentioned previously, there were four anesthetic deaths in this series. Two of these occurred with the use of inhalation and two with spinal anesthesia. The anesthetic mortality rate with both types in this series was 0.3 per cent.

With regard to the pathologic studies of the 1151 cases diagnosed as acute appendicitis, there were 89 per cent which proved to be acute, and these were confirmed by microscopic examination. Of this group, 1007 were examined microscopically. Unfortunately, there can be no satisfactory conclusions drawn from the pathologic reports. This is true because a separate classification has been used in this paper. The chief interest, however, lies in the fact that of the 1007 cases examined microscopically only 143 were reported as essentially normal.

There was one patient in the group who was listed as having actinomycosis of the appendix, and one reported to be tuberculous.

A relatively large number were described as having shown evidence of *Oryzias vermicularis*. In this group, 24 were reported with an average age of 16 years and eight months.

There were eight patients of this series in whom Meckel's diverticulum was found.

Four patients developed herniae following the operation, and all had McBurney incisions. However, it is interesting to note that all had post-operative wound infections.

CONCLUSIONS

A report of ten years' experience with acute appendicitis in a municipal institution has been presented. Six hundred and fifty-one patients were

operated upon during the first six-year period, and without the routine use of the sulfonamides where perforation had occurred. During the subsequent four-year period 500 patients were operated upon, and sulfonamides administered topically at the time of operation if such a condition existed. Following the operation sulfathiazole was given orally in nearly all such cases. The mortality rate is lower in the latter group. Further clinical and experimental studies are necessary in order to determine the value of these observations.

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DISCUSSION—DR. M. J. HENRY, Louisville, Ky.: I should like to discuss Doctor Avcock's paper, since I recently had the opportunity to present a paper on this subject before one of our local societies. The cases I reported were operated upon by Doctor Abell, Sr., Doctor Abell, Jr., and myself. As Dr. Abell, Jr., has been working directly for Uncle Sam, while we have been doing so indirectly during most of the period covered by this study, most of the operations were performed by Doctor Abell, Sr., and myself.

In reading the current literature on the subject one is impressed with the fact that relatively large doses of the sulfonamides are used intraperitoneally. We do not use these drugs in mild cases of acute appendicitis, those in which there is slight extension of the inflammatory process to the surrounding structures. We have used the sulfonamides intraperitoneally in 134 cases, and have divided them as follows:

Acute appendicitis with local peritonitis	15
Appendicitis perforative	32
Appendicitis gangrenous	40
Appendiceal abscess	31
Peritonitis, diffuse	16

Of the 134 patients only one died. This patient was a child age eight, whose temperature was 105.8° F. on the day of operation, who died in less than 48 hours after operation. This child had a gangrenous appendix.

With very few exceptions sulfanilamide was used. Many maintain that sulfathiazole has 50 times the bacteriostatic power of sulfanilamide. We have used it rarely. Practically all cases had five grams of the drug intraperitoneally, very few received additional sulfonamide therapy through the oral or parenteral route. Not as many as five per cent received additional therapy, yet we have a mortality rate of 0.75 of one per cent.

DR. J. C. OWINGS, Baltimore, Md.: Prior to 1940 we used the sulfonamides at the Baltimore City Hospitals only very occasionally, because we had so much difficulty in preventing the drug from caking when sterilizing it. It was known that the powder contained viable spores of various organisms so that we could not use it without sterilizing it. I took this problem to the Hynson, Westcott & Dunning Company, of Baltimore, which developed a granular form of the drug put up in a sterile package that could be shaken into the wound without difficulty. Later we found that we could sterilize the granular form ourselves without any trouble.

My feeling at first was that we had found something very good and that we were going to get excellent results from local application, but in view of what the war has shown in regard to the local use of sulfonamides in open wounds, I am not at all sure of its value. At present I feel that the principal function of local application is that it provides a quick, easy and safe means of raising the blood level at a time when it is often not possible to give the drug orally because of nausea. By applying it intraperitoneally one can raise the blood level and keep it up until the patient can take the drug by mouth. The drug is readily absorbed by this route and its effect is maintained over this critical period.

DR EMIL NOVAK, Baltimore, Md. I should like to say a word about the interesting contribution of Doctor Bunch. One would get the impression from a review of the literature and also from the report which Doctor Bunch made, that perhaps two entities are embraced under the designation of mucocoele. In one we deal with what, to all intents and purposes, is a retention cyst of the appendix. On the other hand, there is another condition which is embraced under this same designation, and is more likely to be encountered by the gynecologist. The mechanism seems to be different, the contents of the mucocoele are not mucin but pseudomucin, chemically readily distinguishable from mucin. The epithelium is of the peculiar very tall "picket" variety which characterizes the pseudomucoid tumor of the ovary, which we believe to be a teratoma. In a teratoma we often find cysts lined with this epithelium, similar to that in mucocoele of the appendix. It is embryologically interpreted as a primitive form of intestinal epithelium. That is one of the reasons we believe these cysts of the ovary are teratomata in which this entodermic tissue has blotted out all other teratomatous elements, just as thyroid tissue does in the so-called struma ovarii. The peritoneal transplants also show the tall "picket" variety of epithelium.

This, then, is a different process from the mucocoele which appears to be simply a retention cyst, we deal here with a pseudoneoplastic or genuinely neoplastic process. Histologically, it is perfectly benign in all cases I have studied, but clinically such cases run an essentially malignant course. When operation is performed one can often scoop out great masses of jelly-like material, but the cells continue to secrete and the gelatinous ascites continues to recur until, often after some years, the patient dies of terminal infection or intestinal obstruction.

The point is that there appear to be two types of mucocoele, but the kind of gynecologist is most interested in is that associated with pseudomucinous cystoma of the ovary. In this, the local epithelium and the character of the exudate appear to be different from that seen in the other variety.

DR R. M. POOL, Memphis, Tenn. During my association with Dr. Lloyd Noland, at Fairfield, Alabama, we observed several cases of mucocoele of the appendix. One of these presented several interesting features. This man was operated upon by Doctor Noland for repair of a right inguinal hernia. A mucocoele of the appendix was found and removed at the same time. There was a granular tumor at the tip of the appendix and, in spite of very careful dissection, a small amount of mucoid material was spilled from this tumor. Doctor Noland recognized it and made a correct clinical diagnosis. The man was operated upon in November, 1927, and made a satisfactory operative recovery in the usual length of time. He returned in the fall of 1931, after a comfortable interval of four years. On examination it was thought that some intra-abdominal fluid could be detected, but nothing was done at that time. In 1932, he was explored because of a large accumulation of intra-abdominal fluid and because an abdominal mass could be palpated. This mass was made up almost entirely of omentum, but practically all the peritoneum was involved in a pseudomucomatous peritonei. The patient died at home in May, 1933.

This case was followed through from the time appendicectomy was performed until the fatal termination, which was due to intestinal obstruction. The pathologic study and the second exploration verified the diagnosis of mucocoele of the appendix with subsequent pseudomucomatous peritonei.

DR R. L. SANDERS, Memphis, Tenn. Since Doctor Bunch was kind enough to invite me to discuss this most interesting subject, I should like to mention briefly two cases of mucocoele of the appendix which have been outstanding in my memory.

The first case was reported before the Louisville meeting of this Association in 1926. The patient, a man, presented a large tumor in the right lower abdominal quadrant. The diagnosis was not made prior to operation, had the patient been a woman, I would have thought the mass an ovarian cyst. It proved to be a mucocoele of the appendix measuring 39 cm in circumference—the largest on record, so far as we could find. It had not perforated, and there were no peritoneal implants. Eighteen years have elapsed since the operation and the patient has had no further trouble. Dr. Hubert Royster was good enough to describe this case in his monograph on the appendix.

The second case was that of a woman, age about 60, who came to Dr. W. J. Mayo during my service with him in 1916. She was found to have a large fluctuating tumor below the femoral ring on the thigh. It was not unlike some of the aneurysms showed yesterday by Colonel Elkin, although there was no pulsation or other evidence of aneurysm. On opening the mass, Doctor Mayo was amazed to find an enormous amount of colloid material, which was coming through the femoral ring. He then explored the abdomen and discovered a large appendix, its tip near the femoral opening. It had perforated and its content was escaping and producing the mass on the thigh. The appendix was removed, the abdomen was closed and the thigh incision sutured. I have not had an opportunity to follow the case, so do not know the ultimate outcome. I am sure Doctor Mayo did not report it, so I am pleased to do so here and to give him the credit.

DR. HUGH A. GAMBIT, Greenville, Miss. I want to confine my remarks to the last paper. For the past 20 years I have advocated the open treatment of peritonitis due to a ruptured appendix. During this time the mortality rate has been 15 per cent in this class of cases. When the sulfonamides came in I found certain disadvantages. One was that it appeared to me there was more oozing in the wounds, adhesions formed more readily, and certain patients had an idiosyncrasy for these drugs. Last year I saw a patient, age 36, in good physical condition, with a ruptured appendix. We would ordinarily have expected him to recover. He was given sulfanilamide, suppression of the urine occurred and he died. I feel that his death was due directly to the drug and that a word of warning should be issued as to the danger incident to its use. I do not feel that the sulfonamides are cure-alls. They have not helped our mortality rate one iota.

Under the open treatment the mortality rate in these ruptured and complicated cases has ranged consistently around 15 per cent. All the patients who died have been more than 65 years of age, with the above exception, some were as old as 85, and many were diabetics. I am definitely assured that we can still keep our mortality rate low without the employment of sulfonamides.

DR. HENRY W. CANN, New York, N. Y. This discussion on the use of sulfonamides, particularly sulfanilamide in its relation to acute suppurative appendicitis, could go on and on indefinitely.

At the Roosevelt Hospital in New York, where we have been interested in the use of this drug intraperitoneally since January 10, 1940—almost five years ago—Dr. Sterling Mueller poured an undertermined amount of sulfanilamide into the peritoneal cavity in a patient who had a ruptured appendix, with diffuse peritonitis. This patient made a very satisfactory recovery. Since that time we have operated upon 1,000 cases of acute appendicitis, and of this number three have died. In this group we have used sulfanilamide intraperitoneally in about 40 per cent, reserving it for the severe cases.

In the five-year period prior to January 10, 1940, we operated upon approximately 850 patients with acute appendicitis, diagnosed microscopically, and in this group 21 deaths occurred.

We believe it is advantageous to use sulfanilamide intraperitoneally in acute inflammatory lesions of the appendix. We have had two experiences with marked jaundice in patients following administration of 10 mg. and 8 mg., respectively. So far as drainage is concerned, we have used drains in 35 per cent of all cases in which sulfanilamide has been used.

DR. HUBERT A. ROYSTER, Raleigh, N. C. I think Doctor Novak has hit the mark in his discussion on different kinds of cysts of the appendix. They vary all the way from so-called retention cysts up to pseudomucinous cysts. We need to consider the pathologic

origin and the location of these cysts. Many of us have encountered small cysts of the appendix under the serosa that have nothing to do with the interior, they are quite common, and have no pathologic significance. On the other hand, cysts inside the appendix of varying size, whether from the mucosa or submucosa, I think represent a degenerative process. In the pseudomucinous cysts we have an entirely different process, classed as an abnormal type, misplaced tissue, and, therefore, coming under the head of teratomata.

In my book (1937) I gave a review of cysts of the appendix including mucocele, if they are harmless, retention cysts or what you please, but the pathologic definition is the discriminating question which applies as we see them clinically. I feel this distinction should be made before we classify any we may see, small or large, which are not simple cysts but teratomata. I think the size of the cyst is important, when it comes to the pseudomucinous variety. I had the pleasure of reproducing Doctor Sanders' illustration in my book, and gave him credit for the largest on record. I have seen none since as large or larger.

Having been retired for six years, I look back on our mortality rate in appendicitis. For several years preceding our retirement we had a mortality of about 15 per cent over the years, and recently I expressed myself to my colleagues as wondering if the improvement since the introduction of the sulfonamides were due to the drug itself or due to good judgment and technic in the operation. I cannot feel that if a man has been operating for 20 years his technic should not improve. I do not think we can attribute all the improvement to the drugs. It is a sad thing that I had to get out before the sulfonamides were invented, I might have assumed none of my patients would die, that to be immortal one should have appendicitis and be operated upon.

DR GEORGE H BUNCH, Columbia, S C (closing). I deeply appreciate the discussion. I wish to thank Doctor Novak for informing us that some adenomatous cysts of the ovary are in reality teratomata. True peritoneal transplants have not been recognized in the cases of pseudomyomatous peritonei reported by me. The cells have not been invasive and masses of adherent pseudomucin could be removed from the peritoneal surface without grossly impairing its integrity.

DR THOMAS B AYCOCK, Baltimore, Md (closing). I greatly appreciate the discussion given this paper. As to the dosage of sulfanilamide, referred to by Doctor Henry, we rarely place more than eight grams in the peritoneal cavity at the time of operation, more frequently we use four or five grams. I think Doctor Owings and Doctor Royster hit the nail on the head in their comment. I do not think any of us are sure where we stand regarding this question—particularly as to the local use in acute appendicitis with peritonitis. I realize, as Doctor Gamble said, that there are dangers in the use of this drug, and we are always on the lookout, blood levels are taken daily in these patients, and always the day following local administration.

SACRAL AND PRESACRAL TUMORS*

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TUMORS which originate in and ventral to the sacrum are so rarely seen that individual experience pertaining to such neoplasms naturally is limited. However, some three years ago, within a period of fourteen months, I encountered three tumors of this region which stimulated my study of new growths of this location. One of these growths was a chordoma, another was an ependymal cell glioma, and a third was a large dermoid cyst.

A few general remarks referable to tumors of this location will be made as a background for the discussion and a brief report of these three cases will be presented. The paper will emphasize primarily the treatment and prognosis of malignant lesions of this region.

The neoplasms of this location are of many pathologic types and usually arise from vestigial embryonic tissue. The potentialities of the sacrococcygeal region are based on the fact that the primitive node occurs here, and from it all the fundamental systems of the body grow forward. During fetal life this remains for a long time a point of fusion of the central nervous system, skeletal axis, segmental musculature and postanal gut. Along the primitive gut wall migrate the primitive cells of the gonad. There are more possibilities here than almost any place in the body. The tumors encountered most frequently in this region are chordomas, dermoids, ependymomas, teratomas, Ewing's tumors, giant cell tumors, neurofibromas and fibrosarcomas. The majority of the malignant lesions will be found to be chordomas, ependymomas, fibrosarcomas, malignant changes in the benign neoplasms of this region and metastases from primary malignancies elsewhere.

The chordoma is probably the most interesting tumor occurring here. It is a neoplasm arising from the cellular remains of the notochord and, therefore, is composed of epithelial tissue. In 1858, Mueller was the first to advance the view that these tumors were of notochordal origin. In 1894, Ribbert confirmed the opinions of Mueller and was the first to apply the name of chordoma to this growth. This was fifty years ago.

The first recorded cases of sacrococcygeal chordomas of clinical interest were those reported by Feldmann and by Mazzia in 1910. According to Mabrey, Wood reported the first sacrococcygeal chordoma in the American literature in 1913. Stewart, in 1922, presented an excellent paper on chordomas and reviewed the literature up to that date. He found only twenty-six such cases in the literature. In 1935, Mabrey again reviewed the literature pertaining to these tumors and found at that time 150 recorded cases of chordoma. Faust, *et al*, in a recent article, submitted 102 additional

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cases of chordoma in the literature. This brings the total number of cases reported to 252 in these two communications.

Most chordomas are situated in the sacral region. The next most frequent site is the spheno-occipital region, although a few cases have been reported along the vertebral column at various levels.

Chordoma may develop at any age. Montgomery and Wolman reported such a tumor in an infant three and one-half months of age, and the oldest case that Chesky found in the literature was in a man age seventy-nine. Dickson and Lamb stated that the average age at the onset of chordomas of this region is from thirty-five to forty years of age, and that males are twice as prone as females to develop these neoplasms. Trauma is considered an etiologic factor in many instances.

Presacral dermoids constitute a fair percentage of the tumors of this region. Whittaker and Pemberton, in a study of twenty-two cases of presacral tumors, reported that nine of them were dermoids.

Presacral dermoids arise from the ectodermal layer. According to Carney, it is possible that dermoids may derive from either of three structures: proctodeal membrane, postanal gut or vestiges of the neuenteric canal.

They may occur at any age. Mannheim and his group stated that no incidence of a presacral dermoid has been found in the male.

Dermoid cysts are usually encapsulated, have a poor blood supply and may compress, but do not invade, adjacent structures. Thomason emphasized that sinus openings in the sacrococcygeal region are usually the external manifestations of cysts or tumors of developmental origin. Lahey and Eckerson concluded that a presacral dermoid should be suspected in patients who have sinuses and abscesses about the anus and who have had repeated operations.

Ependymal cells in the early embryo form a large part of the neural tube. Ependymal gliomas of the sacrococcygeal region arise from remnants of embryologic structures forming the lower end of the spinal cord, the filum terminale, and grow as localized neoplasms destroying bone by erosion. It is the neoplasm which derives most frequently within the sacral canal.

The symptoms produced by early and small growths of this region are usually negligible, whereas those caused by large tumors may be pronounced and disabling. The symptoms are not modified materially by the pathologic histology of the neoplasm because the symptoms of tumors of this region are usually those directly the result of mechanical pressure, that is, pain and anesthesia of variable degrees. This is influenced directly by the size, location, degree of erosion or invasion of bone and extension of the neoplasm. Pain is usually more pronounced in those cases in which the tumor began within or has invaded the bone. Large tumors of this region may cause marked impairment of the functions of the rectum and bladder because of encroachment. This results in the usual symptoms.

A digital examination of the rectum is the most essential part of the

physical examination. The presence of a tumor which displaces the rectum and other pelvic structures anteriorly can be palpated by a rectal examination. The size, contour, consistency and mobility of the tumor can also be ascertained by a digital examination. Roentgenologic findings may be negative or may show erosion, destruction or invasion of the bone. The final diagnosis of the nature of the tumor depends on a microscopic study of tissue from the neoplasm.

Location of the tumor, duration of the growth, size of the neoplasm, degree of extension of the tumor to adjacent structures and pathology of the lesion are factors which modify the treatment and prognosis. The completeness of removal of the tumor and the surgical instrument used for the excision definitely influence the prognosis.

Chordomas of this region occur in one of three locations in relation to the sacrum. The tumor may be retiosacral, within the sacral bone or in, or on the anterior surface of the sacrococcygeal bones. The most frequent site is in or on the anterior sacral wall with the tumor extending forward into the hollow of the sacrum. Adson, Moersch and Kernohan, in a review of nineteen cases of chordomas, found that seventeen originated in the sacrum, involved it and extended into the pelvis. One tumor developed in the sacrum but did not extend into the pelvis, and one developed anterior to the sacrum but did not invade the sacrum. Mabrey reported the incidence of eighty-seven cases of sacrococcygeal chordoma in various regions to be: antesacral 41, retiosacral 29, and central 17.

The duration of the growth naturally influences the size and extent of the neoplasm. According to the case histories, the majority of these tumors have been present for a few years before the patients have come for treatment.

Mabrey found in sacrococcygeal chordomas that the average duration of symptoms before treatment in seventy-seven cases was 35.7 months, or approximately three years. Adson, Moersch and Kernohan reported this figure to be thirteen months. In the case we are reporting, the patient began to have symptoms some five years before admission to the Clinic.

Whereas these tumors are rather slow in growth, some develop to an enormous size. Hsieh and Hsieh reported a chordoma of the gluteal region 20 x 20 x 15 cm. Stewart and Moum reported a tumor 30 x 20 cm and another 26 x 22 x 15 cm. The fact that the symptoms of early disease are negligible probably largely accounts for the long history of the presence of a tumor and explains why the tumor is frequently of large size when a patient comes for treatment. The larger the tumor, the more difficult is its exposure, mobilization and removal. The size and duration of the growth naturally have a bearing on the extent of the lesion. Early and small lesions are usually found somewhat encapsulated, are more amenable to surgical removal and have a better prognosis.

PATHOLOGY

The pathology of the malignant lesion definitely influences treatment.

and prognosis Tumors arising in vestigial structures always present problems in pathologic diagnosis because of their infrequency and because their structure often presents either bizarre cellular pictures of unusual cellular types or mixtures of them The anatomic sites of these neoplasms may help to identify them

Chordomas are soft tumors Their chief histologic features are rounded cells growing in cords and having vacuoles in their cytoplasm or nuclei, accompanied by abundant mucinous material Sometimes they resemble the structure of material from the nuclei pulposi of the spinal column Most chordomas are slow in growth and have a low degree of cellular activity As the tumor develops, there seems to be a predilection to an extension of the growth along the course of the blood vessels and into the adjacent muscles and nerves with an invasion of the bones of this region, rather than a spread of disease by way of the lymphatics The rectum and peritoneum are seldom invaded by the neoplasm These tumors rarely metastasize until late in the disease However, Mabrey found in a review of sixteen autopsies that metastasis was present in 62 per cent of the cases The discouraging fact is that these neoplasms do have a marked tendency to recur locally because of the difficulty of complete, primary extirpation of the disease

Ependymal gliomas occurring here usually simulate closely the cellular pictures of well differentiated gliomas of the brain, in that the cells are evenly rounded, stain well and regularly, have distinct nuclei with sufficient cytoplasm, have a few, light, fibrous trabeculae and show little tendency toward glial fibril formation Ependymal cell gliomas are local, do not tend to metastasize, may show recurrence and usually are of a fairly low degree of malignancy

The dermoid cysts of the presacral area are hard to explain on the basis of anything but vestigial structures Tumors of this type are identified by epidermoid tissues, are frequently cystic and slow in growth Some are teratoid and malignant

SURGICAL TREATMENT

The tumors predominating in this region are either benign or are malignant neoplasms with a low degree of cellular activity A good result can be expected when a benign neoplasm has been removed completely, and low grade malignant tumors should not recur when removed by extending the line of excision well beyond diseased tissue and leaving the field free from contamination by malignant cells

However, practically all reports concerning the cure of chordomas are discouraging This is emphasized by the following observations made by various writers According to Montgomery and Wolman "The ideal treatment for a chordoma is complete surgical extirpation This is almost always impossible It is questionable whether any patient has been permanently cured by operation or irradiation" Chesky stated that the prospect for

complete eradication of the tumor is extremely bad. All patients operated upon, except those seen in recent years, have died of a recurrence. Fletcher, Woltman and Adson pointed out that complete surgical removal of most chordomas is practically impossible. Keane reported that a chordoma is an invariably fatal tumor. Whittaker and Pemberton found the incidence of recurrence is quite high and, if local, is usually due to an incomplete removal of the original growth. Bell stated that no permanent cures of chordoma have been reported. Stewart gave the incidence of local recurrence as 86.5 per cent, and according to Stewart and Morn, thirteen cases out of fifteen who survived surgery are known to have developed a recurrence.

Notwithstanding these discouraging reports, an occasional patient has been known to be alive and apparently free of disease many years after the excision of the neoplasm. Garlock reported a case apparently well ten years after surgery.

A posterior approach with an incision over the sacrum and coccyx extending to near the anus affords the best exposure to tumors of this region. The patient should be in the Kraske position. The coccyx and as much of the sacrum below the sacro-iliac articulation as is necessary for adequate exposure of the neoplasm should be removed.

It is fortunate that a majority of the chordomas of this region occur in the lower part of the sacrum and coccyx, as reported by Mixter and Mixter, for tumors so located are more accessible for removal. Furthermore, it is the opinion of Mixter and Mixter that a rather wide excision of the bones, muscles and nerves of this region should be done when such is necessary for the complete eradication of the disease. They have shown that the segment of the sacrum below the sacro-iliac articulation, together with the coccyx and all of the sacral nerves except the first and second, can be removed without severe disability being incurred by the patient. Bowers confirms the opinion of Mixter.

Wide, radical excision appears logical to me, for although these structures are important, they are not essential to life and well-being. Hence, there should be no hesitancy in sacrificing these tissues when necessary for complete eradication of the disease, inasmuch, as only the entire removal of all diseased tissue offers to the patient a probability of cure.

It is an established fact that the cure of a malignancy depends largely on what is done at the time of the first operation. Malignancies that recur may be retarded in their growth and spread, but are seldom cured by an additional surgical procedure. So again, I would emphasize the importance of making every effort to eradicate completely the disease at the time of the initial operation. All low-grade malignancies that tend to recur locally require a much more difficult procedure with less probability of cure following the second or third excision than would have been necessary at the time of the initial operation.

In keeping with the teaching of my preceptor, Dr. A. C. Scott, Sr., I am convinced that more certain, complete removal of all these low-grade lesions

is attained by the use of the cautery knife for the cutting of all soft tissue, followed by thoroughly baking the bone margin after the removal of all apparently diseased bone. This prevents the transplantation of malignant cells on a raw margin of bone. All regional bony crevices and foramina should also be baked by the cautery in an attempt to destroy all malignant cells burrowing into these regions.

Although I am reporting only two cases of low-grade malignancy of this region so treated, we have found this plan of management favorable in the



FIG. 1.—Roentgenogram demonstrating destruction of the lower segment of the sacrum and coccyx, with irregular bone margins which indicate an infiltrating type of bone tumor—chordoma.

treatment of many neoplasms of low degree of cellular activity elsewhere in the body such as extensively infiltrating basal cell epitheliomas and fibrosarcomas. The cure of such malignancies depends almost entirely on complete local excision or destruction of the disease. It has been our custom to gauge the extent of the excision of such tumors by taking a section for immediate pathologic study from the margin of the excised structures. Any time the frozen section shows the line of excision approaches or extends into diseased tissue the line of excision is modified, when possible, and extended more widely into healthy tissues.

REPORT OF CASES

Case 1—Chordoma. A 44-year-old white female came to the Clinic May 5, 1941. She stated that five years previously she had fallen and injured her coccyx. Since then she had been bothered by a growth beneath the skin over the sacrum. There was no drainage from the growth.

On rectal examination, there was felt a nontender, nodular mass of restricted mobility. It extended from the lower portion of the coccyx up a few centimeters beyond

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the lower margin of the sacrum, thus, making a mass in this region approximately 12 cm in diameter. Laboratory studies revealed essentially negative findings. Roentgenologic examination of the pelvis disclosed that the coccyx and the lower segment of the sacrum had been destroyed by a neoplasm which was thought to be a primary bone tumor (Fig 1).

On May 8, 1941, the patient came to surgery. She was placed in the Kraske position and an incision was made with the cautery knife over the sacrum to within about 2 cm of the anus. The skin flaps were reflected widely and the muscles attached to the lower portion of the sacrum and coccyx were severed approximately 7 cm lateral to these bones. The tumor was thus exposed. It was gelatinoid in appearance, and had



FIG 2—Photomicrograph of chordoma from the sacrococcygeal region

apparently destroyed the coccyx and infiltrated the lower portion of the sacrum. The lower two sacral vertebrae and the coccyx were removed with bone forceps and then the tumor was excised by means of the cautery knife. The exposed sacral bone and the margins and base of the wound were then baked with the cautery. The wound was partially closed after packing the depth of the wound with gauze. The tumor was 12 x 11 x 10 cm and weighed 312 Gm. It was encapsulated, soft and largely filled with gelatinoid material showing few cells. Along numerous fibrous partitions present there were more cells, which were large, clear, pale-staining and sometimes vacuolated. From a strictly histologic viewpoint, this tumor was difficult to classify, but by position, behavior and structure, it was considered to be a chordoma of a low degree of malignancy. The pathologic report was malignant chordoma from the sacrococcygeal region (Fig 2).

From May 23 to June 5, 1941, the patient was given a series of roentgen therapy, the total dosage being 1368 r to the skin. Three months later she reported for check-up. She had a sinus in the sacrococcygeal region which led down to the bone. A sequestrotomy was performed and the sinus was curetted. Tissue which was removed was reported as benign by the pathologist. A second series of roentgen therapy was given, the total dosage being 2000 r. The sacrococcygeal sinus was curetted and packed on two later check-ups, in January and in May of 1942.

The patient has returned regularly for observation and was last seen here September 13, 1944, then more than three years since the removal of the tumor. At that time her condition was satisfactory and by physical and roentgenologic examination there was no evidence of recurrence (Fig 3).

Case 2—Ependymal cell glioma. A white female, age 32, was first seen here on June 30, 1941. For some two years she had had a swelling in the region of the lower portion of the vertebral column. It was tender and caused a dull aching in this region. The symptoms were aggravated by stooping.

On examination, a hard mass about 5 cm in diameter was present posterior to the vaginal vault. It was found, fairly smooth, not very tender, and of rather markedly



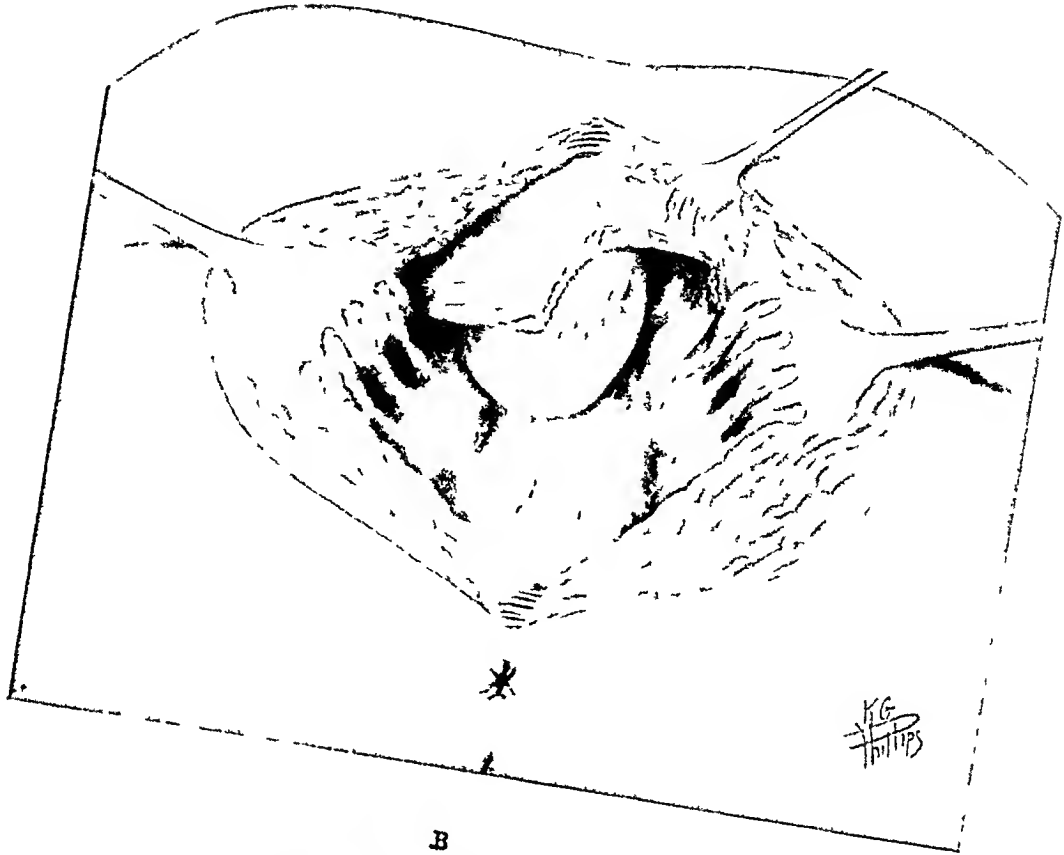
FIG 3—Roentgenogram revealing postoperative resection of the lower portion of the sacrum and coccyx, smooth bone margins and no evidence of recurrence of chordoma.

restricted mobility. By rectal examination it was apparently posterior to the rectum, about 5 cm above the coccyx. The remainder of the physical examination was negative. Laboratory reports were essentially negative. Negative findings were reported following roentgenologic examination of the lumbar spine, pelvis and hips. The final preoperative diagnosis made was of a tumor posterior to the rectum and of probable malignancy.

On July 3, 1941, with the patient in the Kraske position, a cautery knife incision was made over the lower portion of the sacrum and coccyx, the incision extending almost down to the anus. The tumor, 10 x 12 cm in its larger diameter, was exposed anterior to the sacrococcygeal articulation (Fig 4a and 4b). The coccyx and the lower segment of the sacrum were removed. The tumor was well encapsulated except for attachment to the anterior surfaces of the sacrum and coccyx. It was dissected from these by means of the cautery knife and then its attachments in this

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A



B

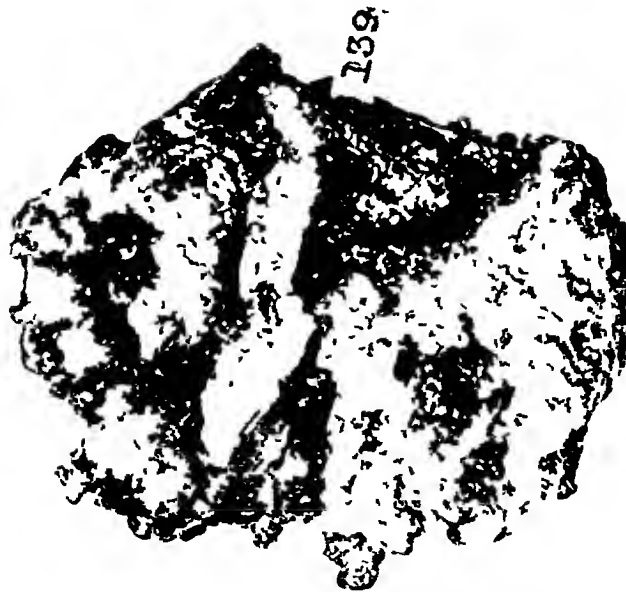


FIG 4—A Drawing of ependymal cell glioma after exposure for surgical removal
B Specimen of ependymal cell glioma after removal

region were thoroughly baked by use of cautery. The excision of the tumor was then completed with the cautery knife. The tumor measured approximately $7 \times 5 \times 3$ cm. It was smooth, fibrous and encapsulated and had a bluish color on the cut surface. The specimen weighed 24 Gm. Sections showed a very cellular neoplasm in which there was an abundant intercellular stroma with many areas of degeneration. The pathologic report was of partially degenerated and infected ependymal cell glioma, Grade I (Fig 5).

She was given two series of roentgen therapy, a total of 2736 r being administered.

She returned for observation November 19, 1941, four months following surgery. At that time a sequestrectomy was performed and the sinus curetted. The pathologist reported that sections showed only subacute inflammatory tissue.

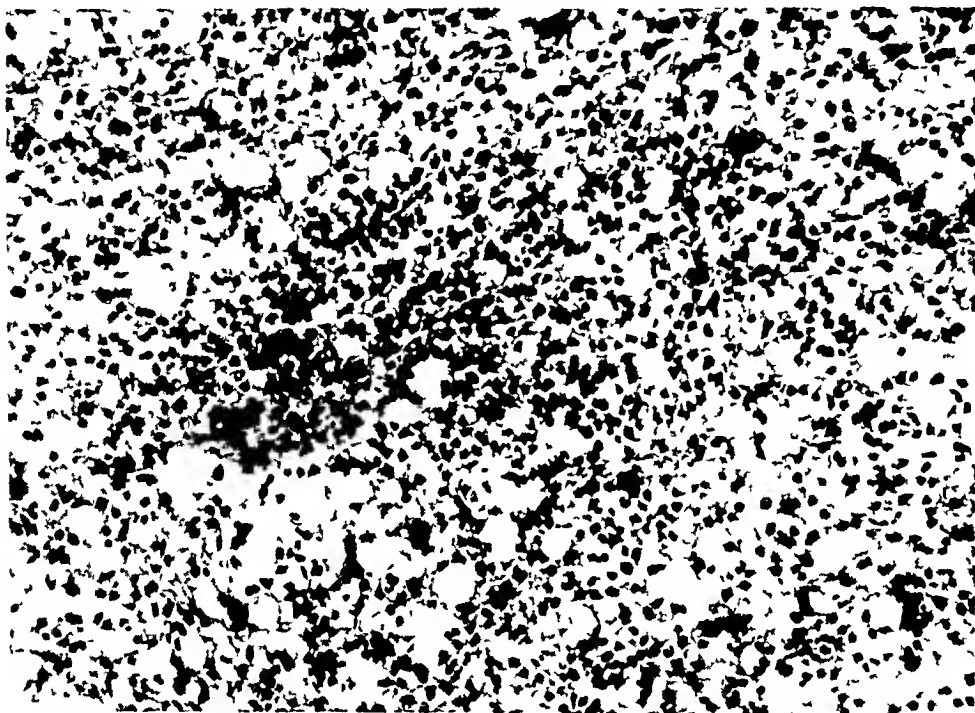


FIG 5—Photomicrograph of partially degenerated and infected ependymal cell glioma, Grade I

The patient returned on June 28, 1943, two years after her primary surgery, complaining of pain in the right buttock region radiating down the right thigh. By rectal examination there could be palpated a mass about 4 cm in diameter anterior to the lower sacrum. Roentgenologic examination showed extension of the malignant process involving the right half of the sacrum up to the level of the sacro-iliac joint (Fig 6). With the patient in Kraske position, an incision was made over the lower portion of the sacrum and practically all of the sacrum below the sacro-iliac joint on the right was removed and the recurrent tumor mass, some 15 cm in diameter, was excised by means of cautery. After excision of the tumor, the margins of the bone and base and the lateral margins of the wound were thoroughly baked with cautery. A third series of roentgen therapy was administered, using a dosage of 1368 r.

The patient returned for observation in February, 1944, at which time a sequestrum was removed. She was last seen here in September, 1944, fifteen months after the excision of the recurrent malignancy. At that time her condition was fairly good. There was no impairment of control of the bladder or anal sphincter. Roentgenologic examination of the sacrum revealed no evidence of malignancy in the bone (Fig 7). There were no enlarged nodes over the body. Rectal examination was negative.

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Case 3—Dermoid cyst The patient, a white female, age 36, reported to the Clinic June 29, 1942. Her chief complaint was of dull, aching and burning pain in the region of the coccyx which had been present for approximately two years.

FIG 6



FIG 7

FIG 6—Recurrence of the ependymal cell glioma two years after the primary excision.
FIG 7—Roentgenogram made 15 months later shows no evidence of recurrence of ependymal cell glioma.

On physical examination, a mass 10 to 12 cm in its long axis and 6 to 8 cm in its transverse diameter was present posterior to the rectum and anterior to the coccyx and lower sacrum. It was irregular, fairly firm, of restricted mobility and not par-



FIG 8—Specimen of sacrococcygeal dermoid cyst

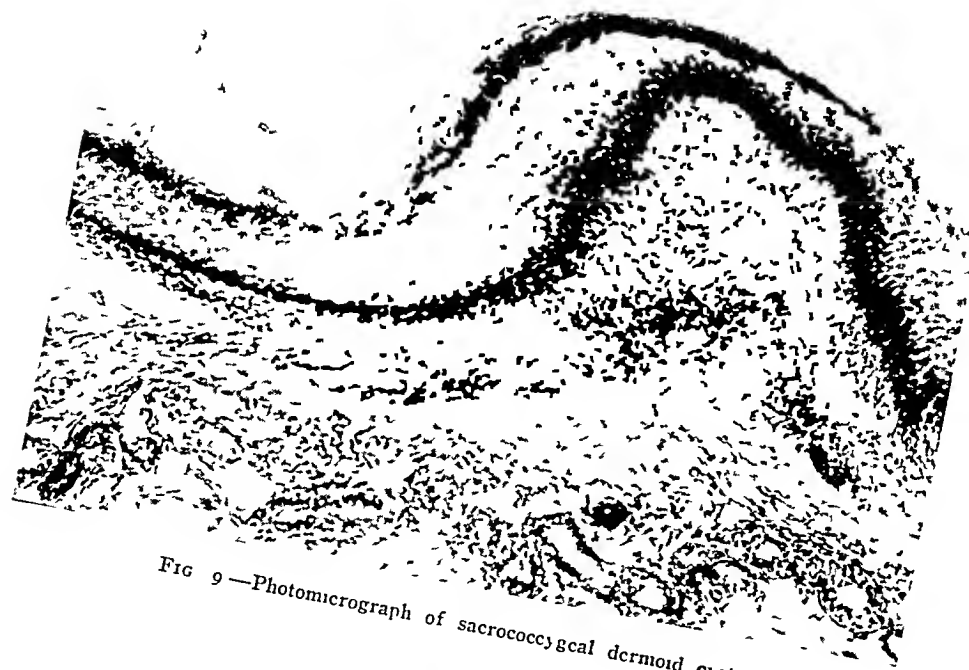


FIG 9—Photomicrograph of sacrococcygeal dermoid cyst

ticulately tender. Findings of laboratory studies were essentially negative. Roentgenologic examination revealed the sacrum and coccyx were negative. A preoperative diagnosis was made of a tumor of the coccygeal region, probably a chordoma.

She went to surgery on July 9, 1942. With the patient in the Kraske position, an incision was made extending from the midsacrum down to within about 2 cm. of the anus. The coccyx and a small portion of the adjacent sacrum were removed. The tumor mass was excised by means of cautery knife and the wound was closed with a drain. The tumor measured 7.5 x 5 x 3.5 cm. and weighed 31 Gm. (Fig. 8). Examination showed a multicystic process with one large space and a number of smaller ones filled with thick putty-colored material of nongreasy type. The lining of most of the spaces was modified epidermis with an occasional accessory structure such as sweat and sebaceous glands. No hair follicles were discovered. The pathologic report on the tissue removed from the sacrococcygeal region was dermoid cysts (Fig. 9).

The patient was dismissed on July 28, 1942, and was last seen here August 18, 1942, at which time her condition was satisfactory.

COMMENT—In the case of the chordoma, complete removal was possible because the chordoma was relatively small. Emphasis is placed on the value of excising widely primary malignancies of low grade which do not tend to metastasize. The use of the cautery knife for the excision is believed to have been a factor in the results obtained in this case. It is my opinion that this patient will probably remain well.

The case of ependymal cell glioma emphasizes the necessity of removing widely all malignant tissue at the time of the primary operation. Certainly a more radical removal of the neoplasm should have been done when the initial operation was performed. Furthermore, even though such a patient develops a recurrence of disease, by a second surgical procedure it may still be possible to eradicate all diseased tissue and thereby cure the patient.

The case of the presacral dermoid indicates that a good result may be expected when the complete removal of a benign neoplasm has been accomplished.

SUMMARY

A majority of the chordomas and ependymomas are malignant lesions of low degree of cellular activity. They tend to recur locally rather than by distant metastasis. According to the histories of reported cases, most chordomas develop a local recurrence. The operative notes for some of these cases state that all apparently malignant tissue was removed by a curette. Curetting a malignant lesion rarely, if ever, results in a cure. The ideal to be attained by the surgical procedure is an initial, complete surgical extirpation of the neoplasm leaving the field free from contamination by transplanted malignant cells. Due appreciation of adequate exposure is important. The sacrifice of important structures must be accepted when necessary for the complete eradication of disease. Much of the lower portion of the sacrum, the coccyx, the lower three sacral nerves and the muscles of this region can be removed without causing severe disability. Recognition of this fact should lead to more radical primary excision of the operable lesions. The use of the cautery knife as the agent for the excision definitely

increases the probability of leaving the field free of transplanted malignant cells. Surgical treatment for these neoplasms based on the above facts will result in a smaller percentage of local recurrence and also will definitely increase the number of patients cured.

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DISCUSSION—DR GEORGE E BENNETT, Baltimore, Md As I look over the audience I am very sorry to see that so few orthopedic surgeons have come in to hear this paper They would learn something if they were present because, by and large, I think we see these cases earlier than the surgeons do As you know, orthopedic surgeons are a clearing house for pain, regardless of where the pain is It has been my privilege to have diagnosed a great many of these presacral and other types of sacral tumors, and I have been much interested in the subject Sacral pain and pain referred to the buttocks often proves to be due to tumors developing in the presacral and sacral region I do not think that orthopedic surgeons, or you as surgeons, should pass up a rectal examination in cases with obscure pain about the sacrum A tumor developing in the posterior part of the sacrum is a problem which should be given serious thought with regard to diagnosis When there is indefinite pain about the sacrum with rather bizarre neurologic signs, or no neurologic signs, the first thing to look for is a presacral, sacral or cauda equina tumor Some years ago I reported a series of cases of cauda equina tumors and called attention to the fact that often the first symptom noted by the physician or surgeon is spasm of the erector spinae and hamstring muscles I do not think this is a subject that we can pass superficially

DR W J MINTIR, Boston, Mass This is a very interesting paper, not only that, but Dr Bennett has added much to the discussion by his remarks I remember his paper which was read in Washington, I believe, and which helped me a great deal

It seems to me that Doctor Brindley has fixed our attention on a small group of tumors which, as a rule, are neglected until pretty late in their history He has picked up three of these, one in a very early stage, for which he is much to be congratulated Most chordomas are higher, but this was low enough to lend itself to complete excision All you can do for most of these is to make a hole and scoop the tumor out and they come back, and that is eminently unsatisfactory surgery He has a cure, and I believe it is going to be complete I wish I could say as much I have one case alive that we hope will be a cure, but I doubt it

There is an interesting group of chordomas of the lower lumbar spine which are sometimes overlooked, many are called hemangiomas It is impossible to eradicate these growths, but they may be treated at times by partial excision, fusion and irradiation

DR JOHN C A GERSTLER, New York, N Y I should like to report two cases The first was a man, aged 64, a surgeon, who, seven years previously had had an episode of left-sided pain, what he thought was a renal colic As a sequela of this attack he had paresthesia of the left great toe and, as time went on, this spread to the anterior crural nerve distribution Being a teacher of anatomy, he followed the spread and distribution of pain very carefully Finally, there was painful paresthesia of the entire left lower extremity, left testis and left half of the penis He sought advice from different clinics, east and west and, finally, was seen in New York by a well known, careful neurologist, who thought he had a lesion involving the cauda equina Some weeks later at a neurologic hospital the cauda equina was explored and nothing was found Several months later, the symptoms continuing, at his own demand, a chordotomy was performed, however, although there was anesthesia to pinprick over the left lower extremity and left lower half of the abdomen, he still suffered agonizing pain—apparently the chordotomy was not high enough

Finally, one day the patient himself pulled on a glove, made a rectal examination and felt a mass, it was a huge tumor filling practically three-fourths of the pelvis Films of the pelvis, made on November 11, 1939, showed a considerable amount of irregular bone destruction in the left side of the pelvis The ilium has been partially destroyed above and medial to the acetabulum The left ischium and the lateral portion of the left pubic ramus are also involved in the destructive lesion A large soft tissue mass is present almost filling the left side of the pelvis"

The patient demanded that something be done, even if it were an interilio-abdominal amputation At another general hospital, as a preliminary step, a Devine colostomy was established A few days later he had myocardial failure and died At autopsy there was found "a sarcoma involving the nerves of the sacral plexus filling the left half of the pelvic cavity and extending into the guteal region"—apparently a neurogenic sarcoma

arising from the sacral plexus. It took the pathologist 45 minutes to get out the specimen. It is doubtful whether surgical removal could have been accomplished. The lungs were free of metastases. My only connection with the case was when, after the tumor's discovery, a trial (under my direction) was given the so-called frozen sleep—cryotherapy*—for relief of his pain. The result was unsatisfactory.

The second case was that of a man, age 64, who had pain only for five or six weeks. Digital examination of the rectum showed an elastic mass in the hollow of the sacrum. Films of the pelvis and colon, made in November, 1944, show "an irregular area of bone destruction approximately 4 cm in diameter situated in the lower portion of the body of the sacrum slightly to the right of midline. A large soft tissue mass lies anterior to this portion of the sacrum and displaces the rectal ampulla anteriorly for a distance of about 5 or 6 cm. Films of the chest show an area of infiltration at the upper portion of the left hilum which apparently represents neoplastic involvement."

In spite of the fact that he had obviously a long-standing involvement, there was only a five weeks' history of symptoms. At a subsequent exploratory celiotomy, the upper border of the tumor was found to be just below the pelvic brim. There were metastatic nodules in the dome and along the free margin of the liver.

The relative rarity of presacral tumors has prompted the reporting of these two cases.

DR G W N EGGERS, Galveston, Texas. I had the opportunity to speak to Doctor Brindley some time ago about these tumors, and I had a case which he requested me to mention today, which is interesting from a diagnostic standpoint. It was a very destructive lesion involving the sacrum. The patient was a young woman who had been advised to have various types of pelvic operative intervention. She had destruction of about two-thirds of the sacrum. The usual roentgenograms of the chest and skull were made, with negative results, and she was advised to have the sacral tumor explored.

I changed the approach a little, making a Y-shaped incision with a transverse incision at the level of the second sacral (that is quite safe) until a positive diagnosis was made. It proved to be a very extensive giant cell tumor from the sacrum itself. The woman was given roentgenotherapy, and regression of the tumor is taking place slowly. One should be cautious in the diagnosis of these sacral tumors.

DR G V BRINDLEY, Temple, Texas (closing). I appreciate these discussions because I know they have emphasized some very important facts. In concluding the discussion I would stress the importance of a complete physical examination and particularly a rectal examination. In a review of the literature it was observed that practically all these tumors had been present for three or five years, or more, when they came to surgery. Certainly, many should have been diagnosed earlier. Had this been done it is probable that more would have been resectable and curable.

Also, I would emphasize due appreciation of adequate exposure even though it necessitates the sacrifice of important structures, recognizing that it is better to accept some impairment of function and disability to obtain a cure. Finally, I would urge the use of the cautery knife for the excision, believing that by its adoption there will be a definitely increased probability of leaving the field free from contamination by malignant cells.

*General Cryotherapy—A Symposium. Bulletin of New York Academy of Medicine, 2nd series, Vol 16, No 5, p 335.

TREATMENT OF VARICOSE VEINS BY STRIPPING, EXCISION AND EVULSION

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AND

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THE CONVENTIONAL MANAGEMENT of varicose veins by high ligation and by injection sclerosis although usually effective has been associated with certain complications and limitations. Local slough, periphlebitis, allergic reaction, deep vein thrombosis, and pulmonary embolism have been reported by Faxon and Barrow¹ Atlas² and others. Painful leg edema and reflex vascular spasm occasionally develop. G de Takats,³ Howard,⁴ Faxon and Barrow,¹ Ochsner and Mahorner^{5, 6} and Sarna⁷ report an incidence of recurrence following combined saphenous ligation and injection therapy of 10.8 to 23 per cent. A period varying from several weeks to many months is often necessary for such satisfactory injection obliteration. Certain patients become discouraged and fail to return for adequate treatment. The incidence of recurrence after injection alone has been between 60 and 98 per cent (Howard, Jackson and Mahorner⁴ and Ochsner and Mahorner⁶).

Many patients request prompt and radical correction of varicose veins to facilitate military or defense appointments or civilian activity. Those with large varicosities have usually been treated in this clinic during the last 27 months by high saphenous ligation, vein stripping, and multiple excision or evulsion of veins, under a general or spinal anesthetic. Pressure bandages have been employed and early activity enforced. This clinical material has facilitated a reevaluation of the effectiveness and the risk of vein stripping. The operation has been employed in 195 patients. One hundred and two of them, treated 10 to 27 months ago, have been carefully followed and will be reported below. The development of the practice of extensive excision of varicose veins will first be reviewed.

THE DEVELOPMENT OF THE SURGICAL TREATMENT OF VARICOSE VEINS

The operative treatment of varicose veins dates back to the time of Hippocrates,⁸ who employed multiple puncture of the veins. Galen, quoted by Aegineta⁹ used a hook to tear out varicosities. Local excision, ligation, incision and cauterization, percutaneous ligation, application of caustics to the skin overlying the veins, injection of various thrombosing solutions, and the application of supporting bandages were all described in the early literature.

Madelung¹⁰ (1884) described an operation for "radical cure" of varicose veins. He completely excised the internal saphenous vein and its associated varicosities through a long incision over the inner aspect of the thigh and leg. This method of treatment was employed in this country in the early twentieth

* Read before the Fifty-sixth Annual Session, Southern Surgical Association, December 5-7, 1944, Hot Springs, Va.

century. It was associated with embolism in 7 per cent of the patients, fatal in 0.7 per cent (Bernsten¹¹). The 14- to 20-day period of bed rest associated with this operation probably contributed to the high incidence of pulmonary embolism. The percentage of cures was high. Schede¹² (1877) described multiple percutaneous ligation. This method of treatment was found inadequate. Peterson¹³ (1893) of Schede's clinic described the procedure which goes by the latter's name. Circular incisions were carried down to the deep fascia on the thighs and legs at several levels. All of the veins encountered were locally excised and ligated. Miller¹⁴ reported a recurrence rate of 67 per cent. A partial or complete Schede incision has since been employed only above ulcers to eradicate venous lakes and communications. Trendelenburg¹⁵ (1891) advocated ligation of the internal saphenous vein in the upper part of the middle third of the thigh and also at times just above or below the internal condyle. Perthes¹⁶ reported a recurrence rate of 22 per cent and Miller¹⁴ obtained similar results in 41 patients.

Keller¹⁷ (1905) reported a method of extirpating the internal saphenous and other large veins by introducing a wire loop or probe upward through the vessel, securing the upper end of the vessel to it, and then withdrawing the instrument and the invaginated vein. He later combined this method with percutaneous ligatures and obtained satisfactory results.¹⁸ Mayo¹⁹ (1906) described a ring vein "enucleator" which he employed in the treatment of varicose veins. The instrument consisted of a ring of steel, about one-quarter of an inch in diameter with a long handle. The incompetent saphenous vein was severed high in the thigh, threaded on to the ring enucleator, and stripped down to the knee. At this point the vein was brought out through a small incision and rethreaded through the stripper. The internal saphenous vein may be stripped to the ankle through three to five small incisions. Mayo also employed a partial Schede incision above large ulcers.

Babcock²⁰ modified Keller's method in 1907, using an "acorn-tipped guide" which was passed down the vein segment, tied to the divided vein, and withdrawn. Friedel,²¹ in 1908, described a more radical procedure, the Rindfleisch-Friedel operation. The internal saphenous vein was excised in the thigh. An incision down to the deep fascia was then made below the knee and continued as a spiral around the leg down to the foot. The veins encountered were ligated and the wounds were packed open to heal by secondary intention.

The importance of the high saphenous collateral circulation was early recognized and combined with radical surgery. Tavel²² (1904) advocated high saphenous ligation above these collaterals. He also occasionally injected phenol into the distal vein segment. Homans²³ (1916) reemphasized the advisability of high ligation and stressed the importance of completely eradicating the internal saphenous vein and its varicose radicles by stripping and excision. The reported results were excellent. Tanner and Fields²⁴ (1927) finding multiple ligation or removal of short sections of veins unsatisfactory advocated removal of the internal and occasionally also the external saphenous

veins from the femoral ring to the ankle. They used a subcutaneous stripper with a small olive tip at one end and a cup at the other. This instrument was passed through the vein segment from below upward. Extraction enucleated the vein without invagination. Satisfactory results were reported. Howard, Jackson, and Mahon,¹ Hoigan,²⁵ and others, advocated stripping from the saphenofemoral junction to the knee and employing injection therapy for the remaining varicosities. Howard, and associates⁴, stated that the complete operation of stripping and excision should be carried out when varicose veins were accompanied by incompetency of both saphenous and perforating valves even though the postoperative disability meant temporary loss of time from employment.

This literature review has demonstrated that radical excision of varicose veins coupled with high ligation is effective. Multiple ligations or circular incisions have given poor results. High ligation and radical excision, as recommended by Mayo, Homans and others, has been employed rarely in recent years because of the associated prolonged hospitalization, the prolonged convalescence, and the risk of emboli or other complications. The extensive literature associated with the practice of high saphenous ligation coupled with injection therapy has been omitted from this review. Complications and loss of time have also occurred following high ligation and injection. The authors have undertaken the present study to reexamine the risk and the effectiveness of radical excision of varicose veins.

The practice of extensive surgical excision or stripping of large varicose veins has been continued by many surgeons. The results have been in agreement with the literature reports. Injection therapy when employed in large varicosities has produced inflammatory reactions occasionally associated with prolonged disability. Repeated treatments have often been necessary. Many patients are unable or are not willing to return for repeated injections although they require prompt elimination of varicosities for military or economic reasons. Radical removal of varicosities seemed desirable. The authors thought that some of the disadvantages of earlier vein excision and stripping techniques might be overcome by supplementing them with elastic pressure bandages and insisting upon early activity. This has now been done in 195 patients. The methods and the results will be reported below.

VEIN STRIPPING TECHNIC

Patients with large incompetent saphenous veins associated with multiple varicosities are selected for operation. The Trendelenburg and the Perthes tests are employed to determine incompetency of the superficial circulation and patency of the deep circulation. Edema, stasis dermatitis, and ulcers if present are treated before operation by supportive therapy and rest. Certain ulcers that fail to heal are compressed preoperatively in the hospital. The course of the veins is carefully marked off with an alcoholic solution of gentian violet immediately before operation. A general or spinal anesthetic is administered. Ultraviolet operating room bactericidal radiation technic is usually

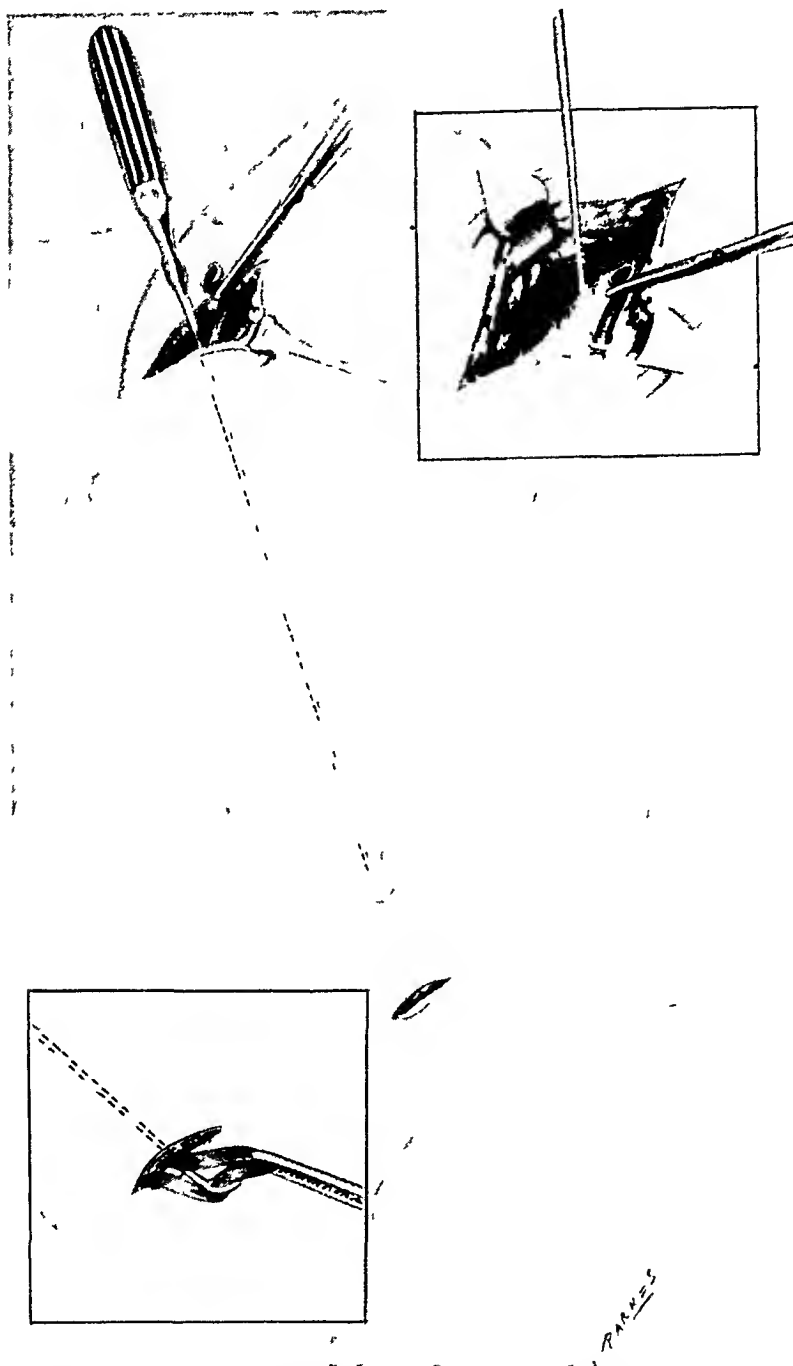


FIG 1—The high saphenous ligation with division of all tributaries, stripping of saphenous trunk in the thigh, and location of the distal vein through a small incision that is performed as a preliminary step in the vein stripping operation

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employed. The lower abdomen, groin, and one or both lower extremities are prepared with an antiseptic agent and draped. The internal saphenous vein is exposed through a small oblique incision just below Poupart's ligament, and dissected up to the saphenofemoral junction. All high tributaries of the saphenous vein are divided and ligated or evulsed. The saphenous vein is

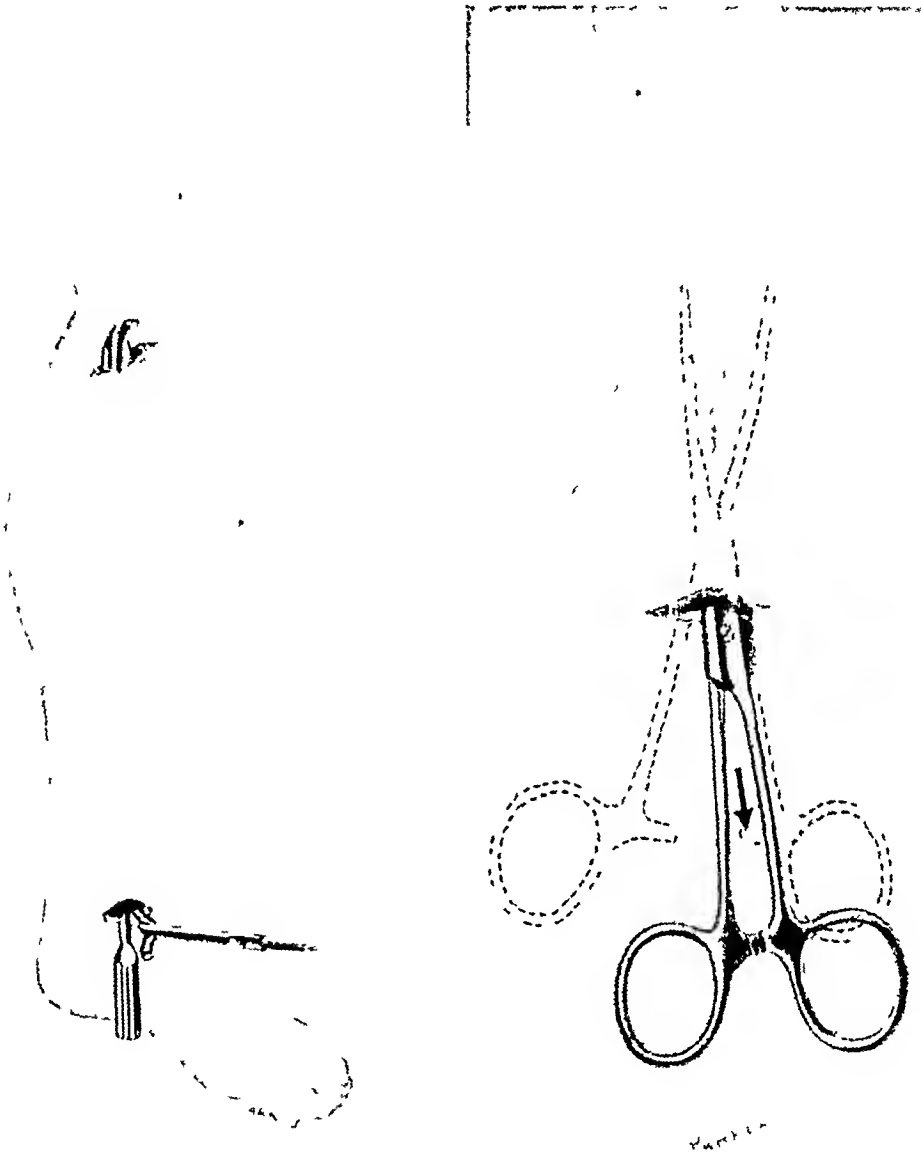


FIG 2

FIG 3

FIG 2—The lower saphenous vein is often located at the ankle near its junction with the medial marginal vein of the foot and stripped upward.

FIG 3—Tortuous and friable saphenous veins do not readily strip and may require evulsion.

ligated and divided a few millimeters distal to the saphenofemoral junction. The distal end of the saphenous vein is threaded through a small-size Mayo vein stripper. The vein is then stripped subcutaneously to the knee and brought out through a short incision one or two centimeters in length (Fig 1). The vein is extracted and rethreaded and stripped downward. If the saphenous vein breaks, the medial marginal vein is located at the ankle and stripped upward (Fig 2). The entire internal saphenous vein can often be removed

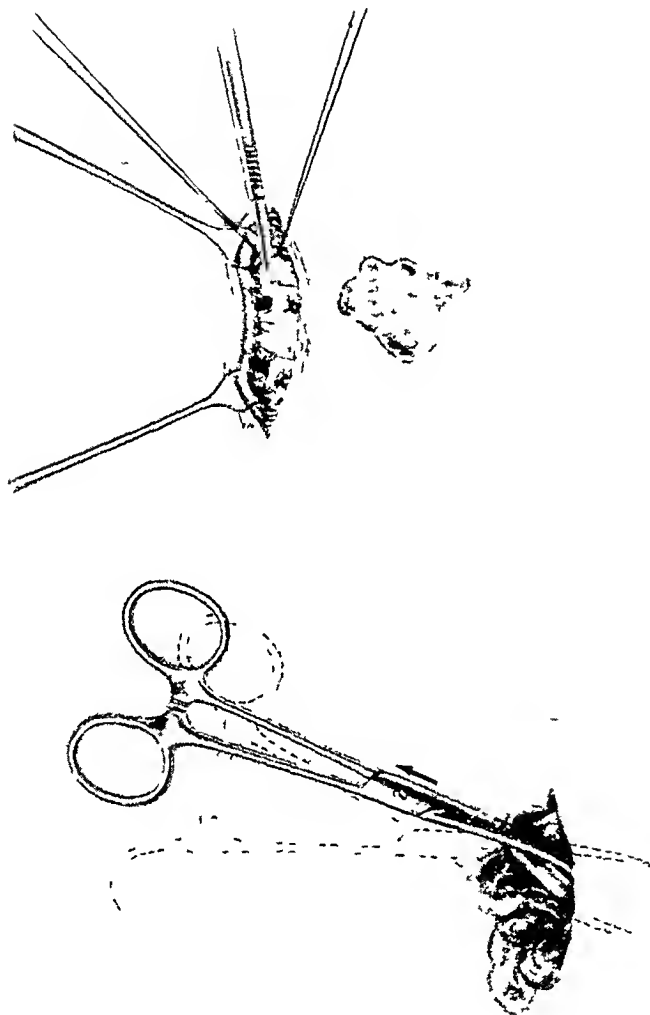


FIG 4

FIG 4—Dissection of localized areas of tortuous varicosities is frequently supplemented by evulsion
 FIG 5—A transverse incision down to the deep fascia dividing veins and avoiding cutaneous nerves
 is often employed above granulating ulcer areas

FIG 5

through four or five small incisions. Tortuous and friable varicosities often cannot be stripped. They are treated by evulsion (Fig 3), or by dissection and evulsion (Fig 4). Bleeding is controlled by pressure applied successively to each operative field. Bilateral varicosities are usually removed simultaneously by two surgical teams. A partial Schede incision (Fig 5) is frequently carried out above areas of stasis dermatitis or ulcer. Open ulcers are occasionally grafted immediately after the vein operation. Blood clots are carefully expressed, the wounds are sutured and dressed, and the extremities are snugly wrapped with elastic bandages. Active exercise is encouraged in bed after recovery from the anesthetic. The patients are usually urged up and out of bed within 24 hours. Elastic dressings are continued several weeks after operation.

THE EFFECT OF VEIN STRIPPING UPON 17 PATIENTS WITH LARGE INCOMPETENT VARICOSE VEINS, WITHOUT COMPLICATIONS

Seventeen patients with large varicosities but without previous edema, ulcer or thrombophlebitis were treated. The operation was the initial treatment in 13. Two had been treated earlier by injection and two by high saphenous ligation. Enlargement of varicose veins had been noticed two to 27 years, average 11, and had been progressing. The usual complaint was leg fatigue. Examination revealed large, incompetent saphenous veins and varicose tributaries. The deep circulation was patent. Communicating veins were frequently incompetent.

These patients were treated by the operative technic described above. They were hospitalized three to nine days, average five. They returned to full activity between seven and 60 days, average 21. Limited activity began several days after operation. The only complication encountered was moderate temporary swelling of one ankle in one patient. Follow-up examination early revealed successful elimination of all varicosities. Eleven patients later developed small varicosities that required occasional injections. Twelve stated that they were greatly improved, five moderately improved.

THE EFFECT OF VEIN STRIPPING UPON 27 PATIENTS WITH INCOMPETENT VARICOSE SAPHENOUS VEINS ASSOCIATED WITH LOWER LEG, ANKLE, AND FOOT EDEMA

Twenty-seven patients with varicose veins associated with edema of the foot, ankle, and lower leg were treated. The edema was moderate in 19 and severe in eight. These patients gave no history of previous thrombophlebitis. Varicose veins and later gradually progressing edema had been present one to 30 years, average nine. Twenty-one patients had been treated only by elastic support. Five had received injection therapy. One had been treated by high ligation. Examination revealed incompetent varicose superficial veins and patent deep veins.

These patients were hospitalized for vein stripping three to eight days, average six, and returned to full activity between four and 42 days, average 20. Partial activity began in the hospital. There were no serious complica-

tions after operation. Early follow-up examination usually revealed satisfactory elimination of all varicosities. Eleven patients later developed venous enlargements. Seventeen of the 19 patients that had moderate ankle edema now have none. Two have some edema, but less than before operation. Four of the eight that had severe edema now have none. Four have reduction of the degree of edema to less than one-fourth of that present prior to operation. Twenty-one patients reported that they were 'greatly improved, four moderately improved, and two unchanged.

THE EFFECT OF VEIN STRIPPING UPON 30 PATIENTS WITH INCOMPETENT VARICOSE SAPHENOUS VEINS ASSOCIATED WITH LOWER LEG AND ANKLE ULCERS

Thirty patients with varicose veins associated with stasis ulcers were treated. Varicose veins had been observed two to 48 years, average 15. Leg or ankle ulcers had been present two months to 42 years, average seven and one-half years. All patients received treatment before vein stripping, varying from bed rest and support through boots, injections, and in five saphenous ligation. Twenty-two also had definite lower leg and ankle edema. Examination revealed incompetent saphenous veins and patent deep veins. Nine ulcers were open at the time of vein stripping. These were skin-grafted immediately after operation in eight patients and before in one. Postoperative boot or elastic support was employed for several months.

The period of hospitalization ranged from three to 53 days, average eight and of partial disability from seven to 120 days, average 36. Early postoperative examination usually revealed that all demonstrable varicosities were eliminated. Thirteen patients later developed small varicose veins. All ulcers initially healed. Twenty-four have remained healed since elastic or boot support was discontinued. Six have recurred and required further treatment. Some edema remained in nine of the 22 patients that had edema before operation. Twenty-two patients stated that they were greatly improved, six moderately improved, and two unchanged.

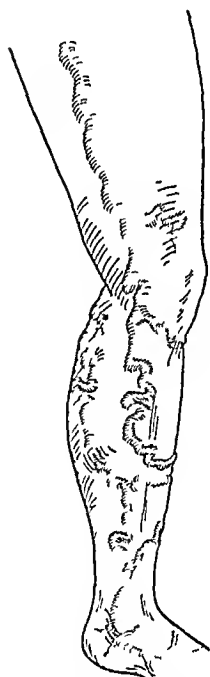


FIG 6 — The usual degree of enlargement of incompetent superficial varicose veins treated in 17 patients by vein stripping and followed for the late effect of operation.

THE EFFECT OF VEIN STRIPPING UPON 22 PATIENTS WITH A PREVIOUS DEEP OBSTRUCTING THROMBOPHLEBITIS

Twenty-two patients that gave a history of an old deep thrombophlebitis beginning with marked inflammatory reaction and edema of the entire leg were treated. The thrombophlebitis was related to pregnancy in nine, abdominal operation in six, trauma in two, typhoid in two, Rocky Mountain Spotted Fever in one, pneumonia in one, and an unknown cause in one. The onset of thrombophlebitis preceded the vein stripping by three to 40 years,

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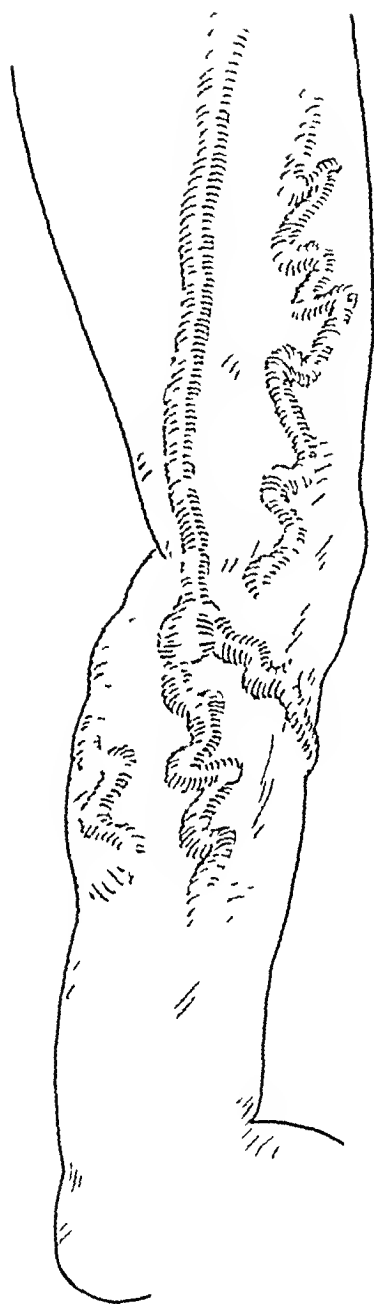


FIG 7

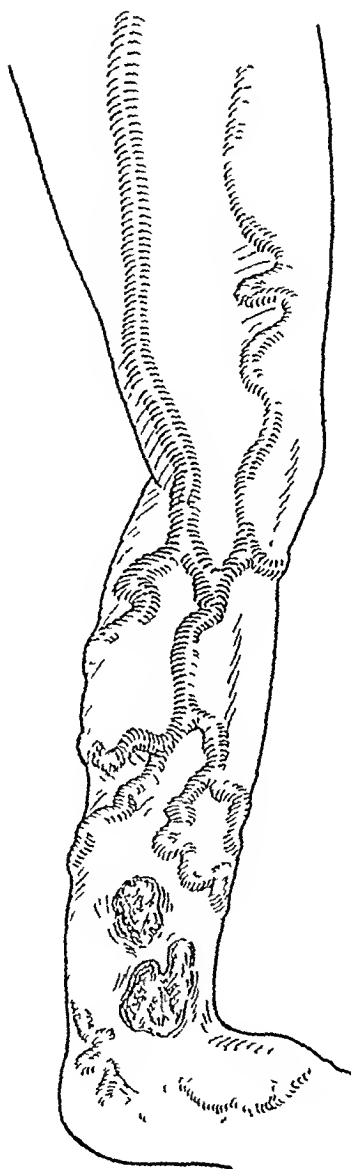


FIG 8

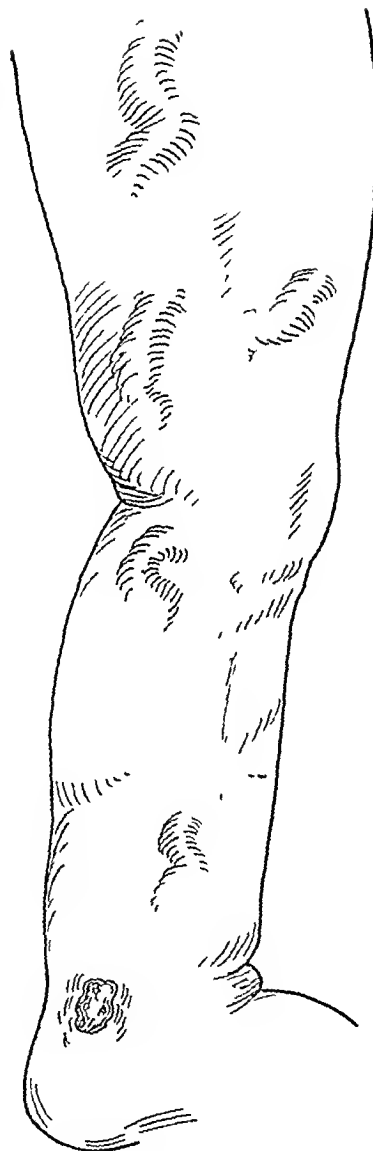


FIG 9

FIG 7—The usual degree of enlargement of incompetent varicose veins and edema treated in 27 patients by vein stripping

FIG 8—The usual degree of enlargement of incompetent varicose veins and the usual type of ulcer present in 30 patients treated by vein stripping

FIG 9—The usual degree of leg edema present at the time of vein stripping in 22 patients that had a previous deep obstructing thrombophlebitis

average 16. Two patients had noticed varicose veins before the thrombophlebitis. The remainder developed varicose veins and complications late after the thrombophlebitis. All patients had leg edema. Sixteen had had ulcers eight months to 30 years, average 10 years. All patients had been treated by bed rest, supportive boots, or injection therapy, and seven had had in addition high saphenous ligation. The tourniquet tests revealed incompetent superficial veins and patent or probably patent deep veins. Nine patients had open ulcers at the time of operation.

The period of hospitalization for vein stripping ranged from five to 19 days, average eight. The period preceding return to regular activity ranged from five to 90 days, average 37. Ten of the 16 ulcers have remained healed since operation. Six have recurred in spite of continued conservative care. The leg edema has disappeared in 13, decreased in five, and remained unchanged in four. Small new varicosities have developed in 13 patients. Thirteen of the patients stated that they were greatly improved, eight moderately improved, and one unchanged.

THE EFFECT OF VEIN STRIPPING UPON SIX PATIENTS WITH LARGE INCOMPETENT VARICOSE SAPHENOUS VEINS AND MISCELLANEOUS COMPLICATIONS

Two patients entered the hospital with bilateral large incompetent varicose veins present many years and complicated during the preceding week by the development of a clot of phlebothrombosis, six or seven inches long, in the dilated saphenous trunk of one leg. This developed just above the knee in one patient and just below in the other. Inflammatory induration was present about the clot and lower leg edema had begun. Deep veins were patent. Both patients were treated by bilateral high ligation and vein stripping. The clotted areas were partially stripped, partially dissected, and partially evulsed. The patients were out of bed within 24 hours. The areas of excision of the phlebothrombosis healed quickly. Lower leg edema did not recur.

One patient was treated for varicose veins that had developed in edematous ulcerated legs during 25 years of intermittent and varied treatment of a severe burn of both legs. Numerous skin grafts applied to the several ulcers had disappeared following return to activity. Bilateral vein stripping followed immediately by skin grafting effected complete early healing. One year later the ulcers and the edema had recurred.

Three patients with definite familial and congenital edema of the lower legs associated with enlarged incompetent varicose superficial and patent deep veins were treated by stripping. The edema, late after operation, was unchanged in one patient, somewhat increased in one, and improved in one. New large varicosities developed within a year in each patient.

SUMMARY

One hundred and ninety-five patients with large incompetent leg varicosities have been treated during the last 27 months employing high ligation, vein stripping, excision and evulsion of veins, pressure bandages and early ac-

tivity. This procedure was applied simultaneously to both legs in 147 patients, to one leg only in 43, and to one leg with high saphenous ligation of the other in five. There has been no operative and no late mortality from the procedure or from complications of varicose veins. Clinically recognizable pulmonary embolism did not occur.

A few patients developed surgical complications. One obese patient had a cardiac decompensation and oliguria that responded to treatment within one week. One had a large inguinal incisional hematoma that subsided spontaneously. Five patients among 25 operated upon with open ulcers and others with some degree of stasis dermatitis developed subcutaneous localized abscesses that required treatment. The transverse Schede incision, when employed frequently, opened and healed by secondary intention. Occasional patients developed small hematomas in the subcutaneous defects produced by the stripping. These absorbed spontaneously.

One hundred and two of the 195 patients treated between 10 and 27 months ago have been carefully followed and reexamined. They have been described above in five separate groups. In all groups demonstrable varicosities have been eliminated by the operation except for occasional overlooked varicose tributaries. Small new varicosities appeared later in 51 of the 102 patients. A few of these became large enough to require treatment by limited surgical excision or by injection. Lower leg, ankle, and foot edema was present in 77 patients. Late examination revealed no edema in 49, improvement in 21, no change in 6, and increased edema in 1. Lower leg or ankle ulcers present in 47 patients responded to preoperative treatment in 28 and were open and skin grafted at the time of operation in 19. Thirty-four have remained healed since operation and 13 have recurred although reduced in size. Seventy-one patients stated that they were greatly improved, 24 that they were moderately improved, and 7 that they were unimproved.

Recently the vein stripping procedure has been extended to include patients with less advanced pathologic change. The period of hospitalization in this group was 3 or 4 days and the period of limited activity 7 to 10 days. The results were uniformly satisfactory.

CONCLUSIONS

High saphenous ligation, vein stripping, and either excision or evulsion of veins combined with pressure bandages and early activity has proved effective in the treatment of a group of patients with advanced pathologic change associated with large varicose veins. It has, in the opinion of the authors, been more effective than ligation and injection therapy used earlier in patients with similarly advanced pathologic change. Although the operation has exposed large areas of skin and was often carried out in the presence of granulating open ulcers, it has been performed with a low rate of infection. Pressure bandages and early activity may account for the absence of pulmonary embolism or deep vein thrombosis. The appearance of new small

varicosities in one-half of the patients within the short period of observation covered in this report suggest that some defect of the remaining veins or abnormality of circulation must exist that is not entirely corrected

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DISCUSSION.—DR. HOWARD MAHORNER, New Orleans, La. I want to congratulate Doctor Grimsom on his results. He has certainly carefully tabulated and evaluated these and no one could expect better results. I cannot, however, agree that stripping is very often indicated. It is generally known that high ligation alone is not the entire treatment for varicose veins, and that multiple ligations and segmental excisions are frequently indicated. I think the type of operation chosen must be adapted to the case in question and one should not expect too much in the absolute prevention of any evidence of recurrence such as mild ectasias. Doctor Grimsom found some mild evidence of recurrence in an appreciable percentage of their patients. This simply emphasizes the fact that by surgery one can cure the varicose veins but not the tendency to varicose veins. Moreover, no type of operation establishes the normal physiology.

Some of my friends have spoken to me favorably of stripping, and I do not disagree that it might be an advantage in certain cases. However, I prefer to divide the operations indicated into five types depending on the degree of varicosity and the complications (slide). In the first group, sometimes with large varicosities when the retrograde flow is only through the saphenous, a single ligation is all that is necessary. If the patient is past middle age, he will not develop varicose veins again, if he is younger, he may. If there is retrograde flow from the deep to the superficial veins below the main opening of the saphenous, an additional ligation above the knee is necessary. In some instances, if the varices are large, excision of segments is indicated, sometimes even on the outer side of the thigh. When varicose veins are extremely severe and retrograde flow occurs at various levels in the leg, these leaks may be determined by the comparative tourniquet (Mahorner-Ochsner) test. In such cases one should attempt to stop such abnormal flow, and it is not feasible to tie off each little communicating vein. Just remove the segment into which they are leaking. It is sometimes essential to cut out scarred areas in the region of the ankle and regraft that particular part.

I am sure stripping of the veins should never be forgotten because it has merit in some cases, but the point I wish to make is that no one operation should be used and adapted to all the cases one encounters.

DR. H. M. SCHIEBEL, Durham, N. C. I would like to say a few words about our work along this line. I have been much interested in varicose veins for about 13 years, since I was put in the Vein Clinic at Baltimore some years ago and had to dress ulcers all morning time after time. We became awfully tired of this, and I am sure every one here has had about the same experience. From that time on I have been consistently interested in something that would cure these people. I do not think we wish to say, however, that we have found something which is completely curing these patients. We have used a series of different methods in trying to cure them. We have tried high ligation, multiple ligations, removal of segments, and still do these procedures on patients when we think these operations will eradicate the pathologic condition. We do feel, however, that the old operation of stripping these veins, which was almost completely discarded, should be given more attention in treating some people who are really bad varicose vein patients.

We have learned something else from this procedure. There have been many theories about the formation of varicose veins and we do not know the cause, but we have learned one thing by actually examining the long segments removed. We have seen that there is a remarkable absence of the normal number of valves in these veins. Our pathology department reports that these patients have from one-fourth to one-sixth the normal number of valves, and this may be something added to our knowledge of these patients. In our follow-up we notice that we see little spots appearing here and there, more often in the young than in the old. On the other hand the results are better in the young with severe varicose veins than in the old patients, for the reason that there has been less edema and, therefore, little or no pathologic change in the skin and subcutaneous tissue.

With regard to hospitalization, we have frequently heard the comment by the proponents of simple ligation and injection that it is not necessary to hospitalize their patients. We want to say that it has not been necessary to hospitalize ours very long. Some of our house officers and nurses have had veins treated by this method and they are back working early. One nurse went back in four days, she did not work full time, but did some of her work and did not wish to stay off duty. She was not uncomfortable, and she wanted to move about.

DR. KEITH S. GRIMSON, Durham, N. C. (closing). The comments of Doctor Mahorner and the illustrations of his technics for surgical excision of varicose veins are welcome. Large localized varicosities may well require excision. Vein stripping and vein evulsion as employed in our study is a rough rather than a precise form of surgery. It has, however, facilitated elimination of extensive varicosities not easily accessible for nice dissection. Injection therapy used earlier for large varicosities was associated with foreign body reactions and other complications more troublesome than those associated with vein stripping.

QUADRICEPSPLASTY*

LT COL T CAMPBELL THOMPSON, M C , A U S

WASHINGTON, D C

FROM THE WALTER REED GENERAL HOSPITAL ARMY MEDICAL CENTER WASHINGTON, D C

THE RESIDUAL DISABILITY following any severe injury to an extremity is just as often due to loss of function of the soft parts as to malunion, nonunion, or infection of the bones. Malunion can usually be prevented and is not difficult to correct. Nonunion can be overcome by bone grafts even when there has been considerable loss of bone. Infection can be prevented or eliminated by sulpha drugs and penicillin provided sound surgical procedures

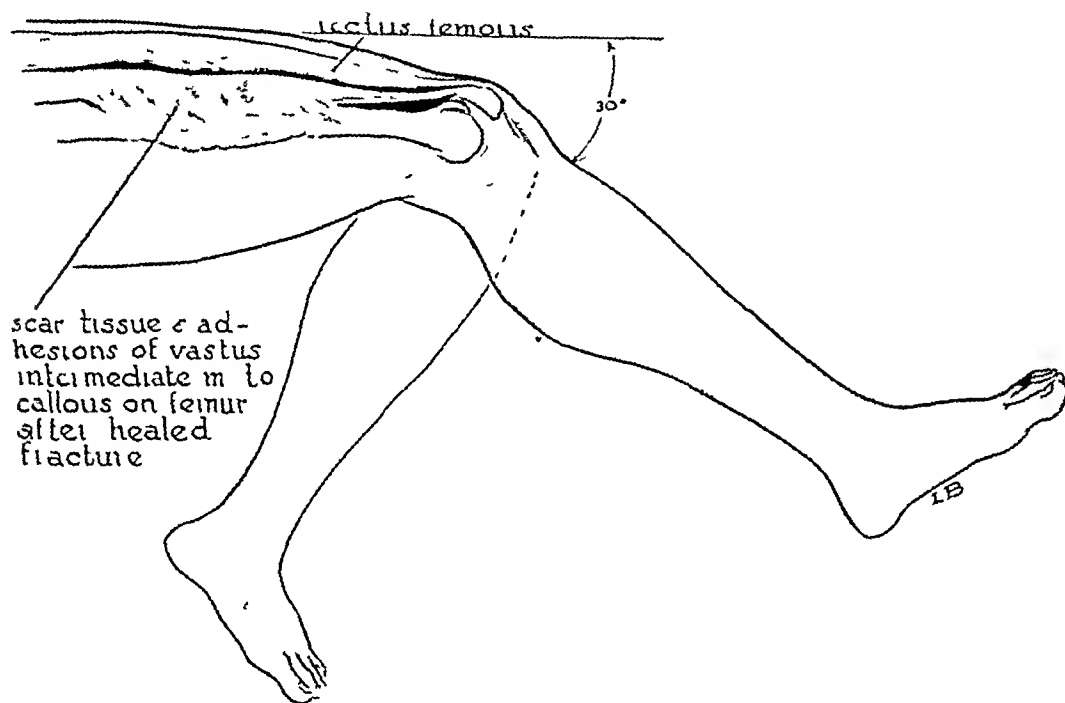


FIG 1—Drawing illustrating adhesions between quadriceps and adjoining muscle

have not been neglected. Soft-part injuries heal rapidly as compared to fractures but complete restoration of normal function is rarely attained. Plastic surgery has accomplished wonders in correcting deformities due to extensive skin loss but when tissues with very specialized functions are replaced or surrounded by scar tissue, considerable loss of function is inevitable.

Reducing scar formation to a minimum is the secret of success in nerve suture and nerve grafting. Restoration of function in a repaired or transplanted tendon can never be obtained if there is scarring between the tendon and the surrounding structures.

* Read before the Fifty-sixth Annual Session of the Southern Surgical Association December 5-7, 1944, Hot Springs, Va

FIG 2

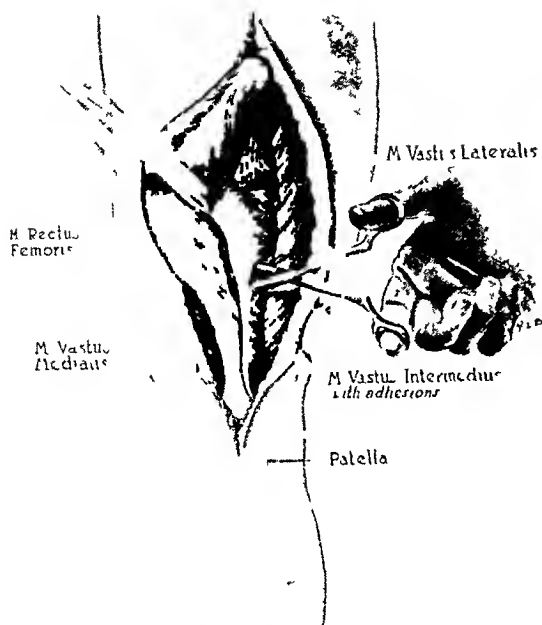


FIG 3

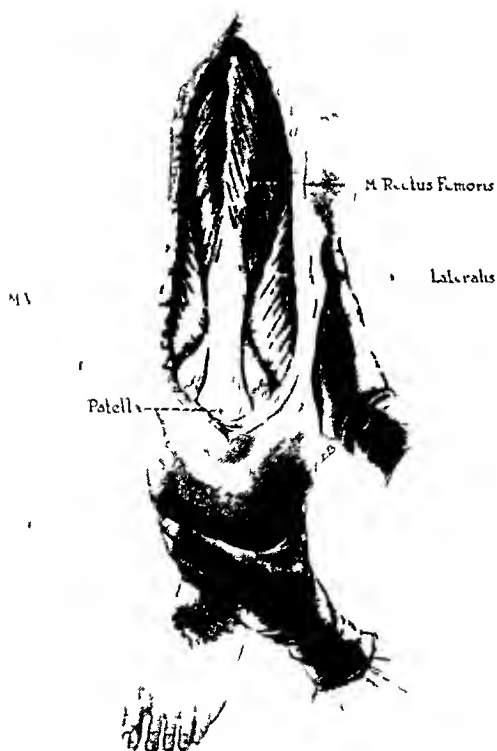
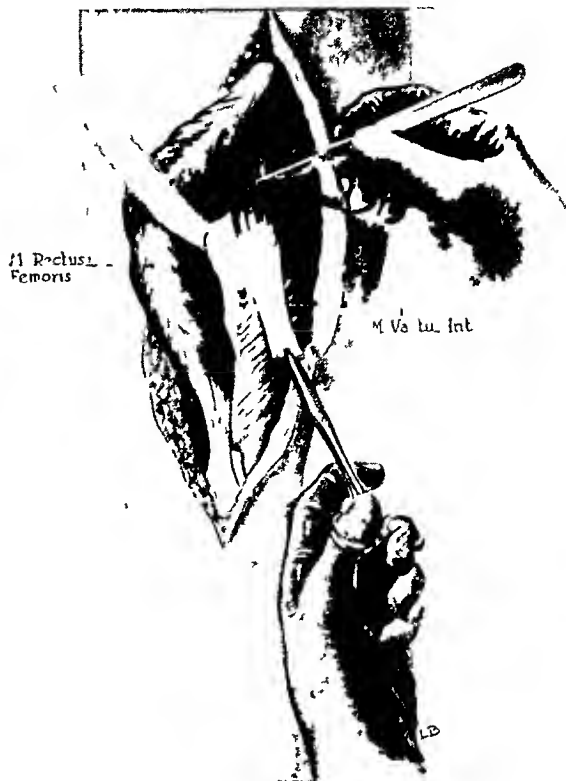


FIG 4

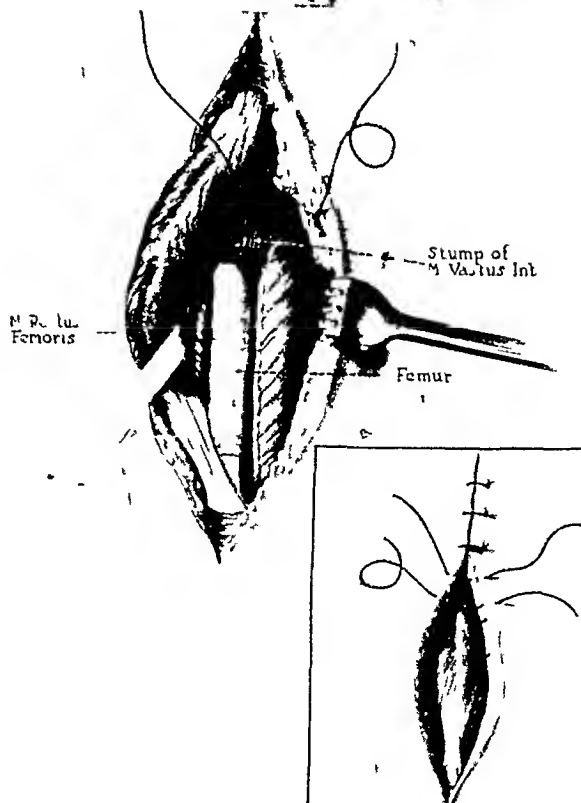


FIG 5

FIG 2, 3, 4, 5—Illustrating the steps in the operative procedure

QUADRICEPSPLASTY

When one considers that the fundamental characteristic of a muscle is its power to enlarge in its transverse diameter while it shortens in length, it is obvious that any scarring or fibrosis either in or around a muscle will so



FIG 6—Illustrating degree of flexion obtained



FIG 7—Illustrating amount
of extension

effectively reduce its activity that the range of motion in the joints controlled by the muscle will be drastically curtailed or even eliminated. The excision of the scarred portion of a muscle or the isolation of a normal muscle from

surrounding scar tissue will often result in marked improvement in both active and passive motion of the joint controlled by the muscle. The principle of excision or isolation of scar tissue can be used in any part of the body. The motion picture which follows shows how it can be applied to the extensor mechanism of the thigh.

The shaft of the femur is almost completely surrounded by the vastus lateralis, vastus medialis, and vastus intermedius. Any injury to the thigh, especially a compound fracture due to a missile injury, will cause scarring and fibrosis in one or more of these muscle bellies. The loss of extensibility of any of these muscles will effectively limit knee motion by anchoring the patella to the femur. Manipulation in an attempt to improve flexion is very apt to result in fracture of the patella. The rectus femoris muscle is more superficial than the rest of the quadriceps and often escapes injury. It is longer than the other components of the quadriceps mechanism and can be dissected away from them without destroying its nerve and blood supply.

In the operative procedure to be shown the scarred vastus intermedius is excised. The knee is then flexed to 90 degrees, or beyond, *without lengthening* the rectus femoris muscle. If either of the remaining vastus muscles is badly scarred it is isolated from the rectus femoris muscle by making a new intermuscular septum of soft tissue. The intact rectus femoris permits *early active motion* and is the reason why most of these patients have regained full active extension.

Nineteen patients have been operated upon with very satisfactory results in all, as far as increase of flexion is concerned. Two of these patients with extensive scarring of all components of the quadriceps muscle, including the rectus femoris, have not regained full active extension. This could scarcely have been expected.

This principle of radical excision of scarred muscle and isolation of active muscle from scar tissue has also been applied to the shoulder, elbow, wrist, and calf.

CONCLUSIONS

- 1 Excision of scar tissue from a muscle increases the extensibility and contractility of the remaining muscle.
- 2 The interposition of normal tissue between normal muscle and scar tissue allows the muscle to function more effectively.
- 3 The application of these two principles to thigh injuries results in remarkable improvement in knee function.

DISCUSSION—DR GEORGE E. BENNETT, Baltimore, Md. Of course you all understand it is a great pleasure for me to open the discussion on this paper. Lengthening the quadriceps is one of my babies. I did my first case in June, 1917—about 27 years ago. The operation was simply the application of an old surgical principle in a new location. Colonel Thompson's quadricepsplasty is again the application of an old surgical principle. He selects a type of injury of the femur and muscles which results in tying down of the vastus intermedius and by removal of the scarred area the leg can be flexed to approximately 90 degrees without disturbing the rectus muscle and speeds recovery to

QUADRICEPSPLASTY

full extension of the knee joint, which has been one of the drawbacks in quadriceps lengthening. I have made some modifications in the original technic described and practiced in selected cases. It must be borne in mind, however, that Colonel Thompson's tenoplasty is not applicable to muscle shortening in the lower third or upper third of the femur. I should like to congratulate him on this splendid paper.

DR PAUL B. MAGNUSON, Chicago, Ill. This paper of Colonel Thompson's, with presentation of his method of lengthening the quadriceps, has been extremely interesting. It would be informative if we could go into the causes which bring on the necessity for the operation described by him. I cannot resist saying that incision through the middle of the quadriceps is the cause in most cases and that in most instances the operation should never have been necessary.

I could not help noticing that the manipulation was rather aggressively performed, but I know that Colonel Thompson is very careful about this manipulation, and that it is done slowly under very well-controlled force. If it is not, there is serious danger of fracturing the femur just above the condyles, especially if the leg has been non-weight-bearing for some time and there exists the atrophy of disuse. Overzealous manipulation is to be avoided.

I think Colonel Thompson's adaptation of Doctor Bennett's original procedure is well thought out and well executed.

LT COL J. C. THOMPSON, Washington, D. C. (closing) I wish to thank Doctor Bennett and Doctor Magnuson for their remarks. I do not claim any originality for this procedure, but the fact that part of the muscle can be left intact does help a great deal in early restoration of function. So far as the cause of a stiff knee is concerned, I think there will be some limitation of knee motion following a fracture of the femur no matter what form of treatment has been used. In my experience, there is more stiffness following multiple pin fixation than any other type of treatment. It is practically impossible to put a pin into the femur without going through the quadriceps. Although these patients do move their knees, they do not move through a full range. There is always some fibrosis and consequent restriction of motion. Most of the cases in these series have resulted from severe compound fractures, usually with extensive soft tissue injury. Some have had loss of muscle, draining sinuses, and scars, which have required a number of operations to obtain healing. In such cases one must do what he can with what is left. We could go on and on about the correct treatment of fracture of the femur, but that is not our thesis today.

MEMOIRS

HERMANN BERTRAM GESSNER

1872—1944

FOREWORD I deem it particularly fitting that I should pay a tribute to the memory of Dr Hermann Bertram Gessner, who was first my intern, then my assistant, later my colleague and for fifty years my loyal friend



Doctor Gessner's professional career began as an intern at the Charity Hospital of New Orleans in the fall of 1895, when he was assigned to my service in the surgical division of the Tulane University, to which I had been appointed chief that year, as the newly elected Professor of Surgery. The professional relations there established continued as an uninterrupted and warm friendship for over half a century when his untimely death on August 31, 1944, severed the link that for so many years had united our interests in the same tasks, whether in the clinic, at the bedside, in the classroom or in the operating theater. In these relations, the official differences in rank and age as between Chief and Intern, Professor and Student, Senior and Junior,

played no part, because lines of demarcation were never visible in an association characterized by mutual affection and respect *

* * *

HERMANN BERTRAM GESSNER was born in New Orleans on February 19, 1872. His father, George Gessner, born in Bavaria, came to America in 1853. As a student at the University of Wurzburg, he participated in the uprising for a Constitution that took place in Germany in 1848. From 1853 to 1907, Professor Gessner taught the classics and German in New Orleans, with the exception of his period of service in the Confederate States Army with the Washington Artillery, from 1862-1865. While his teaching was principally in the form of coaching private pupils, he taught also in several schools, including Tulane University which, in 1906, gave him the degree of LL.D. Doctor Gessner's mother, née Josephine Nicks, came to New Orleans from her native city of Bremen in 1850, when she entered the school of the Ursuline Convent.

After attending various private schools, Doctor Gessner entered the High School of the University of Louisiana, which was soon to become the Tulane University. In 1889, he received the degree of A.B. "with distinction." In 1891, that of A.M. Also, in 1889, he shared the Judah Touro Medal for Greek with another classmate. During this period, he became a charter member of the Louisiana Alpha Chapter of Phi Delta Theta. Later, he was elected a member of Phi Beta Kappa. After two years in the Medical School of Tulane, he entered the Charity Hospital as resident student and ambulance surgeon, one of six successful aspirants out of forty in the annual competitive examinations.

As an undergraduate intern, he showed so much efficiency that he was appointed "Chief of Clinic" (equivalent, at present, to clinical assistant) in my service at his graduation 1895. In this position, Gessner soon developed the qualities of system, method, and precision which had distinguished his father, the famous Professor Gessner as a teacher of languages in New Orleans. In fact, Hermann the son was a remarkable example of the transmission of hereditary traits and aptitudes, for, even as a school boy, he had already acquired a very correct knowledge of German from his father and almost as good a knowledge of French from his mother, who, though a native German, had been educated in French at the Ursuline Convent in New Orleans. Besides an unusual linguistic memory, Gessner had been thoroughly drilled in the principles of language and the fundamentals of grammar by his father, a rigid disciplinarian in the study of basic philologic principles, as became a professor brought up in a German university. With grammar as a key, Gessner acquired Spanish and the rudiments of the

* Doctor Gessner was the first in a long list of young men who gave me the benefit of their service, their loyalty, their talent and the vigor of their youth in helping me to discharge my mission as a teacher of surgery during the 32 years of my professorship at Tulane. For all these, living and dead, I retain ever-green and grateful memories.

Romance languages with ease, an acquisition which in later years served him in good stead by developing a clientele among the Latin-American residents of this city. His philologic aptitudes were also a great help to him by his mastery of German, which had become so essential to Medicine at the time of his graduation. The Germanophile wave which had begun after the Franco-Prussian war (1870-71) had gained great momentum during the Bismarckian period, sweeping over the medical literature and thought of this country and centralizing all postgraduate medical education in Vienna and Berlin, the dual Mecca of all medical graduates who could afford to travel. During this period, German was at a premium and German teachers and translators were in demand. No scientific article seemed complete without a reference to the current German literature. Every young writer who aspired to scientific recognition had to show his proficiency in research by his fluent citations of the *Zentralblatts*, *Jahresberichts*, *Beitrages*, *Wochenschrifts*, *Archives*, *Ergebnisse Sammlungs* and the what-not of the elaborate catalogue of the classified periodical German literature. In fact, no man was worth talking to on any scientific subject if he could not quote German authority. Those who could not were antiquated or out of date. All this was before 1914-1918 when the Americans learned that they did not have to cross the ocean to worship in Aesculapian shrines. From this viewpoint alone, it is evident that Gessner's thorough mastery of German was of incalculable advantage to him, not only by adding considerably to his academic height among his scientific friends but by notably increasing the circle of his clientele.

Despite his attainments in the humanities, Gessner never obtruded his superior knowledge and culture except on rare occasions when some obnoxious bombast in the class needed a fine needle-prick to deflate his bulk, a few murmured words quoted from Latin or Greek by Gessner sufficed to collapse the balloon.

He was elected demonstrator in the laboratory of operative surgery in succession of Dr. W. S. Bickham, the very capable first incumbent in this department, whom Gessner had assisted for two sessions. From demonstrator he was soon promoted to the professorship of Operative Surgery, serving in this capacity from 1900 to 1907, when he was elected professor of Clinical Surgery, which he held until September 1, 1936, when compelled to resign by ill health. He was my senior assistant in the operating room at Charity Hospital and at Touro Infirmary from 1895 to 1905, after which he became senior associate surgeon on the visiting staff at the Touro Infirmary—a position which he retained until 1936. In 1889, he took a very active interest in the teaching of oral surgery at the New Orleans College of Dentistry, later the Dental Department of Tulane University, which he had largely helped to organize.

In 1905, he spent several months studying the histology of tumors with Doctor Bloodgood at Johns Hopkins Hospital. In 1907, he studied in London, chiefly in the clinics of the West London Hospital.

Despite the great demands made on his time by his teaching and hospital

duties and rising practice, he contributed many valuable papers which were largely read at the proceedings of the local parish, state and regional societies. These were largely based on the observations and experiences that he shared with me as my senior assistant at the Charity Hospital and at Touro Infirmary. Quite apart, and in addition to, the regular routine of appendicectomies, hernioplasties, gallbladder and stomach operations, he took special interest in the treatment of aneurysms, in which he became an early pioneer by following closely in the wake of my operations in which he participated as my assistant. In this way, he became an expert in the technic, as shown by his paper entitled, "My Experiences in the Matas Operation of Endo-aneurysmorrhaphy" (*New Orleans Med & Surg Jour*, 67, 598, January 1915) in which he reported seven operations for aneurysms of the lower extremities, including three cases of arteriovenous fistula, without a death or disability attributable to the operation. He was the first surgeon in Louisiana to repeat my experience and results in endo-aneurysmorrhaphy for arterial aneurysms (June 20, 1904) and in the cure of arteriovenous fistula (May 30, 1908) by the Matas-Bickham transvenous technic, as described in the *ANNALS OF SURGERY*, May, 1904.

His "Experience with the Matas-Allen Aluminum Band as a Test of the Collateral Circulation in the Circle of Willis" in dealing with the ligation or occlusion of the common and internal carotids (*Southern Med Jour*, 5, 307-31, June, 1912) was a very conclusive demonstration of the practical value of the band in giving timely notice of acute cerebral ischemia following the occlusion of the artery. This paper and his report of cases of elephantiasis and lymphedema as a supplement to my first paper on the condoleon operation as applied to nonfilarial elephantiasis (1913) were the outcome of our collaboration at the Touro and at Charity Hospital. Apart from this, the subjects of his papers were largely suggested by his observations and reflections on the diseases most frequent in our southern subtropical environment as exhibited in our large Negro services at the Charity Hospital, namely, abscess of the liver, elephantiasis nostras, anhrun, actinomycosis, and the problems of surgical tuberculosis, cancer, tetanus, traumatism of the bones and joints, gunshot wounds of the heart, chest and abdomen. His teachings as demonstrator of operative surgery also led to his special attention to the methods of local and regional anesthesia which were such a distinct and absorbing feature of our clinic in the first three decades after Koller's discovery of cocaine (1884), transfusion, methods of amputation arthroplasties, plating of fractures and skin grafting, which are all reflected in his "Laboratory Guide," published in 1906. He also did experimental work on the circulation of the testis in connection with cryptorchidism and the operations for its correction (1912, 1913). It is remarkable that with his great ability for bibliographic research, the list of his publications is not more extensive, amounting to about eighty-five papers and addresses, which appear in the transactions of the local, state and regional societies of which he was a member. They are almost all contained in the official journals, the *New Orleans Medical and Surgical*

Journal, the J A M A, the ANNALS OF SURGERY, Southern Med Jour, and others * Gessner's aim in writing was very much as his oral teaching—chiefly directed at lucidity, brevity and correctness, without display of ornamental bibliographic erudition. This anomaly in a man of his scholarly taste is accounted for, partly, by the fact that bibliographic research was very expensive in New Orleans in the earlier years of his practice. The local library was very scant in texts and periodicals (the German especially) for a young doctor struggling for a living and caring for the needs of a growing family. In fact, to do any work of consequence required frequent visits to the Surgeon General's Library at Washington, which was time-consuming as well as expensive—all of which accounts for the general penury in the medical literature of the South from the end of the Civil War to the first decade of the present century. In addition to these obstacles in Gessner's case was the consciousness of his cardiac disability at a time when he could have contributed much more of his mature learning and experience.

As a surgeon, Gessner's excellent anatomical and technical foundation made him accurate, deliberate and safe, bold when necessary, but not adventurous. Always keenly sensitive of his responsibility to his patients and, as an honest teacher to his students, he gave much time to the preparation and after-care of his patients. Naturally reserved and serious-minded, he never indulged in levity or coarse remarks, he gave dignity to the operating room and to surgery without pretentious solemnity. He was uniformly kind and gentle to all his patients, the Negroes, who contributed the bulk of his surgery at the Charity Hospital, always rejoiced when he made his rounds. He had the human touch and earned loyal friendships from the humbler ranks of life. As a teacher, simplicity, method, clarity, precision gave special value and impressiveness to his lectures and demonstrations as well as to his discussions at the meetings of the medical societies.

Activity in medical organization characterized Doctor Gessner's professional life from the first. He was a member of the Orleans Parish Medical Society (President, 1902), Louisiana State Medical Society (President, 1930-'31), Southern Medical Association, Fellow of A C S and for twenty-seven years a Fellow of the Southern Surgical Association. All of these societies particularly of the City and State, show in their proceedings distinct evidence of his animated and unfailing participation in their work. Deeply interested in the Charity Hospital and in the efforts of the Visiting Staff to secure recognition in the management of the professional side of the Institution, he was Chairman of the Conference Committee of the Visiting Staff from 1913-1915.

He served as an acting Assistant Surgeon, U S Army, in the Spanish-American War of 1898, and as First Lieutenant in the Reserve Medical Corps of the U S Army in 1916, on the Mexican Border. There were also two temporary Service connections with the U S Health Service in 1897 and

* A complete chronologic bibliography, with copies of reports, are available at the Rudolph Matas Library Medical School, Tulane University of Louisiana

in the historic antimosquito campaign of 1905 which put an end to all yellow fever visitations in New Orleans

Ever conscious of his duties as a citizen, he unfailingly qualified as a voter by registration and payments of poll tax, he cast his vote in every contested election, strong in his convictions, always in the lead as a supporter of good government and of every civic and cultural movement that tended to advance the welfare of the community

Long-time a member of the Unitarian Church, he was a devoted worker in its fold and held practically all the offices, including the presidency, that the congregation could give to its communicants. Deeply religious in a reverent, cosmic sense, and a liberal and humanist, as said by his Minister at his obsequies, "There was no dogmatism in his religion, instead, there was tolerance and mercy and tenderness and justice"

Cardiac disease, the tragedy of his life, came relatively early at the age of 57, in 1929 to influence his career by imposing a disability which ultimately robbed him of a full decade of activity in his profession and of the most useful years of service to the community

A ruptured appendix and peritonitis, complicated by a widely diffused thrombophlebitis came in 1935 to add new burdens to the crippling effect of his previous cardiac disability, compelling him to retire altogether from practice and resign all his professional appointments. In 1936, a year after this event, the Faculty conferred on him the title of Emeritus and the Charity Hospital and Touro Infirmary that of Consulting Surgeon. Despite his disabilities and compulsory rest during the ten years of his retirement, he kept in touch with the literature of the profession and especially its all-absorbing social, economic and legislative problems. He found great recreation in the company of his friends and those who assembled regularly at the Round Table Club, of which he was president (1937-38), where he promoted and shared the spirit of good fellowship to the very end

Another side of his life was known only to his close friends. He loved the outdoor life and enjoyed the opportunities that his retirement gave him to indulge in fishing—his favorite sport—which had been denied him in the busy days of his practice. The folklore of the bayous and of the swamps which he gathered on his fishing trips interested him, and the comrades who accompanied him brought back stories of "the grand old man who would sit listening to the swish of the water and talk about the stars"

His illness, which had been fairly well tolerated during the years of his retirement, grew rapidly worse in the last few months before his death, culminating in violent attacks of angina pectoris, which ended fatally in the afternoon of August 31, 1944. At the autopsy, which was held in accord with his long expressed wish to his wife, the presence of a large organized, partially calcified mural thrombus was revealed in the left ventricle, which partly filled the ventricular space. The thrombus had followed a cardiac infarct in the ventricular wall at the time, no doubt, when he felt the first pain of angina fifteen years before his death. There were also evidences

of coronary disease and of other secondary visceral lesions but in the opinion of his physicians and pathologists (Drs Randolph Lyons, Lawson, and Friedrichs) who performed the autopsy, the thrombus was the prime cause of his death. His tolerance of this remarkable concretion for so many years was in itself a valuable contribution to the pathology and prognosis of heart disease, it fully justified his insistence on a postmortem investigation. Also, as evidence of Doctor Gessner's calm and deliberate contemplation of his approaching end was his request that his remains be cremated and his ashes strewn on the ground where his father had been buried thirty-seven years before him.

Thus ended Dr Hermann Bertram Gessner, a fine, intellectual and honored citizen, an excellent surgeon and a teacher of genuine distinction in his art, a scholar of high attainments whose merit will always be remembered by the thousands of the students and others who profited by his knowledge and example during the forty years that he was a teacher in the schools. Personally, as I knew him, he was the incarnation of honesty, absolute integrity. Incapable of insincerity or of shallow snobbish pretensions, always affable, approachable and self-contained but never exuberant, he was very firm in his convictions which were not easily displaced once he had arrived at them. He possessed a quiet dignity without austerity, which commanded confidence and respect of his colleagues and laymen alike. It has been well said that Doctor Gessner's personal friends were as numerous as his acquaintances and his death has brought sorrow to many. A devoted husband and affectionate father, he was particularly zealous to see that his children were given the best educational opportunities. As told by his oldest daughter, "he accepted the older pattern of discipline, but mellowed through the years and was more indulgent to his grandchildren than as a busy Surgeon he had had time to be with his children."

He is mourned by his wife, née Jessie Hayes, of Lake Charles, Louisiana and four children, Leonard E, Josephine H (Mrs Austin Ferguson), Barbara J, and Commander Edward H Gessner, USNR, whose distinguished service in Normandy Beach, Cherbourg, Newfoundland and other Battle Fronts, have won him high distinction as a brave and resourceful Commander in the Naval Service of the Nation.

To his wife, his children and grandchildren, he has bequeathed an imperishable inheritance of honesty, intelligence and character far more precious than "towers of gold or pyramids of old."

RUDOLPH MAIAS

EDWARD PEIRSON RICHARDSON

1881—1944

Edward Peirson Richardson was born in Boston, April 4, 1881. His father, Maurice Howe Richardson, became Moseley Professor of Surgery at the Harvard Medical School and Chief Surgeon of the Massachusetts



General Hospital. His mother was Margaret Peirson, who came from a prominent New England family, some of whom were physicians and surgeons. Edward, the eldest of six children, decided early to follow in his illustrious father's footsteps. He graduated from Harvard College in 1902 and ranked first in his class at the Harvard Medical School, which gave him a doctor's degree in 1906.

His career was closely associated with the Massachusetts General Hospital and the Harvard Medical School. Working his way from "House Pupil" through the Outpatient Department, he finally in 1927 became John Homans professor of surgery and chief of a surgical service at the

Massachusetts General These final appointments were on a full-time basis, which meant the abandonment of a very large private surgical practice

Richardson contributed extensively to the surgical literature His publications were mainly in journals but include a book, written with J H Means as coauthor, on the thyroid gland He had an interest in all phases of medicine in a broad sense He performed all surgical procedures with deftness and ease but was particularly interested in abdominal and thyroid surgery

In addition to the Southern Surgical Association he was a member of the American Surgical Association, the International Society of Surgery, the New England Surgical Society, the Society of Clinical Surgery, and the Boston Surgical Society

Richardson was a clear-thinking, observant clinician whose diagnostic acumen was outstanding He never made a showy impression, keeping in the background, modest to a fault, yet held the profound respect of his associates He was a natural surgeon, developing a technic of gentleness combined with accuracy and reasonable speed His teaching was of the type that made students and junior staff listen, since every word carried a knowledge of the literature and from a vast experience he was able to separate important data from the whole

In 1915, he went to France with the first Harvard Unit No 22 General Hospital, British Expeditionary Forces When the United States entered World War I, he served with the American Expeditionary Forces in France and Germany in 1918 and 1919, being honorably discharged with the rank of Major

In 1917, he married Clara, the daughter of the late Dr Frederick C Shattuck—for many years Jackson Professor of Clinical Medicine of the Harvard Medical School and chief of the East Medical Service of the Massachusetts General Hospital This was a happy union and to them were born three sons the eldest, bearing his father's name, has graduated from the Medical School and finished part of his postgraduate training prior to entering the Armed Services Mrs Richardson's untimely death in 1923 following cesarean section was doubtless a secret source of pain and suffering for Edward, but at no time was this evident to his friends

Edward gave the impression of a recluse to those who did not know him well As a matter of fact, he loved life and people and never missed a well-earned holiday with his friends on field and stream or club He was a fair shot, could throw a fly with expertness, and enjoyed golf His endurance and lack of apparent fatigue made it difficult for those of us, who saw him daily, to realize that his brilliant career could be cut so short

At the age of forty-nine, while teaching a group of students, cerebral hemorrhage occurred which disabled him so much that he was not able to take up professional work again He never regained adequate speech but understood all that was said to him and frequently attended local surgical meetings after his accident He laboriously taught himself to read again

and to write with his left hand. He took up painting as a hobby, traveled a good deal with his boys, and enjoyed fishing to a considerable extent. He bore his affliction with a fortitude seldom seen. Never a word of complaint was heard nor an impression of bitterness given. This made his friends appreciate more than ever the true worth of the man.

Shortly after a second cerebral hemorrhage January 26, 1944, Edward died. His passing will be long felt by those who knew and loved him. Mankind lost a champion surgeon, a great leader, and students a brilliant teacher.

ARTHUR W. ALLEN, M.D.

KENNETH HAZEN AYNESWORTH

1873—1944

DR. KENNETH HAZEN AYNESWORTH, member of the Southern Surgical Association, died October 30, 1944, at the age of 71 years. The cause of his death was apoplexy. He is survived by his widow, Mrs. Maude Brian Aynesworth, two sons, Kenneth H. Aynesworth, Jr., and Major Brian Aynesworth, now serving overseas with the United States Army Corps, two daughters, Mrs. Wilson Crosthwait, of Waco, and Mrs. Thomas Clifton Mann, of Washington, D. C., and two brothers, Dr. Horace T. Aynesworth, of Waco, and Levan Aynesworth, of Fresno, California.

Doctor Aynesworth was born in Florence, Texas, on February 9, 1873. He attended Baylor University at Waco, Texas, and received the degree of Doctor of Medicine from the University of Texas in 1899. He was awarded the honorary degree of Doctor of Laws from Baylor University in 1933. He did postgraduate work in Berlin in 1908-09, and also attended graduate courses at Johns Hopkins.

Doctor Aynesworth began the practice of medicine in Waco, Texas, in 1903, and continued to make this city his home until the time of his death.

Doctor Aynesworth showed a great deal of enthusiasm about everything he did. He was strong in his likes and dislikes. He was active in a number of scientific societies, as well as medical organizations. He contributed a number of scientific papers, including papers read before the Southern Surgical Association.

He had many interests outside of his profession. He was an archeologist of some note and a collector of historical relics, as well as a collector of books and pamphlets on the history of the Southwestern part of the United States. He donated a large and valuable library upon the history of Texas and the Southwest, with many Indian archeological specimens, to Baylor University at Waco. He seemed to care for neither wealth nor fame but was very much in love with his work.

Doctor Aynesworth served on the Board of Regents of the University of Texas for a period of eleven years. He was a member of the American Medical Association, Southern Surgical Association, the American College of Surgeons and the American Board of Surgery. He was one of the



founders and past president of the Texas Surgical Society. He was a member of the Alpha Omega Alpha, honorary medical fraternity, the Texas Academy of Sciences, Texas State Historical Association, West Texas Archeological and Paleontological Association, and founder and member of the Philosophical Society of Texas.

He will be very much missed by the members of the Southern Surgical Association.

ALBERT O. SINGLETON, M.D.

WILLIAM SIMPSON ELKIN

1858—1944

THE INVITATION to contribute lines to the memory of a life-long friend an intimate professional and business associate, is a duty and responsibility not unmingled with overwhelming personal emotion. This friend is Dr William Simpson Elkin, born April 26, 1858, in Lancaster, Ky, and who died in Atlanta, Ga, April 24, 1944, almost on the eve of his eighty-sixth birthday.

The son of a prosperous farmer of Garrett County, he was thoroughly prepared to enter Centre College, Danville, Ky, and, in 1879, received his A B degree. Three years later, 1882, his medical degree was conferred by the University of Pennsylvania. The rapidly growing City of Atlanta attracted him, and there he made his home until his death.

On October 26, 1887, he married Miss Nellie Duncan, of Lancaster, Ky. Their only child, a son, died in infancy. Mrs. Elkin died January 1, 1934. In October, 1935, he married Miss Nell Warren Osborne, of Stamford, Ky, who still survives him.

His nephew, Dr Daniel Collier Elkin, is now Colonel and Chief of the Surgical Service in the Ashford General Hospital, White Sulphur Springs, W Va. Doctor Elkin early developed a marked ability as a surgical clinician in the out-patient department of the Southern Medical College. In a few years he was promoted to Professor of Clinical Surgery and attending Surgeon of the Grady Memorial (Municipal) Hospital, of 400 beds. Following the consolidation of several medical colleges, he became Dean of the Atlanta College of Physicians and Surgeons, and from time to time, in conjunction with Dr Abner W. Calhoun, Professor of Ophthalmology, contributed large sums in support of this institution.

The death of Dr Hunter P. Cooper in 1906, and coowner of a private sanatorium, resulted in the formation of a partnership with the writer. He succeeded Doctor Cooper as Professor of Obstetrics and Gynecology. Sensing the spirit of the times, Doctor Elkin envisioned radical enlargement of hospital teaching facilities, and the absolute necessity of becoming an integral part of a viable University. Quietly and alone, he interested the Candler family, wealthy benefactors of the young Emory University (the parent Emory College at Oxford, Ga, 40 miles distant) and, in 1915, the renamed Atlanta Medical College became the Medical School of Emory University. The writer is confident that no other man could have so aroused the enthusiasm and interest in such a huge and mutually advantageous enterprise, in securing donations and an endowment of millions of dollars. Upon his retirement in 1925, the degree of LL D was conferred by Emory University, and, in 1929, a like degree honored him by Centre College.

Doctor Elkin was a deacon of the First Presbyterian Church, Director of

the First National Bank, a Mason, a Democrat, and a member of several exclusive social clubs. He was a member of the Southern Surgical Association since 1890, a Founder, in 1913, of the American College of Surgeons, twice past President of the Fulton County Medical Society, and, of course, affiliated with the district, State and National organizations. He enjoyed a handsome income from a large city practice and a State-wide consultation clientele, and by thrift, and unusual business sagacity, amassed a comfortable fortune.

Doctor Elkin's standard of citizenship was high. All worthy religious, civic and charitable projects found his purse open, and he often remarked that it was the obligation of every good citizen to register and vote for the lowest to the highest office. He invariably evinced anger when anyone, legally eligible and physically fit, endeavored to avoid jury duty. There was no personal political ambition in him, although he was often invited to participate in conferences in various legislative bodies because of his unusual sound sense and forthright principles. Golf finally lured him from the exactions of his professional work. His great personal charm and camaraderie in the enjoyment of congenial companionship on the links gave his fellow players unforgettable pleasure.

Other than an occasional trip to Europe and winter cruises in the Caribbean, or a few weeks at Palm Beach, the outstanding event in the last half of his life was the Kentucky Derby week, where for many years he maintained a large box and dispensed gracious hospitality to a wide circle of friends.

The death of Dr. William Simpson Elkin marks the passing of an irreplaceable friend, a wise counselor, and, in the opinion of the writer, the greatest all-around Doctor he has ever known.

WILLIAM S. GOLDSMITH, M.D.

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PREPARATION OF BATTLE CASUALTIES FOR SURGERY

LT COL HENRY K BEECHER, M C , A U S

CONSULTANT IN ANESTHESIA AND RESUSCITATION
MEDITERRANEAN THEATER OF OPERATIONS

IN CARING for the man wounded in battle we are at first concerned solely with what he needs to make it possible for him to withstand transport to the hospital and then to meet the stress of emergency surgery. All else, even the question of ultimate survival, is secondary. The conditions that are to be overcome, the increasing forces that must be opposed, and the means used are the subject of this report. Conditions within the patient arising directly from the wound as well as adverse external circumstances that influence his condition will be discussed, but the emphasis here is on treatment.

THE WOUNDED PATIENT

The enemy has produced the worst wound he could, and its consequences are cumulative—dehydration increased by unusual fluid loss in sweat and vomitus, continuing hemorrhage or plasma loss, pain making rest impossible, increasing emotional exhaustion, developing infection—these and other factors are set in operation by the initial wound. Their progress in the seriously wounded is to be checked in most cases only by surgery or by death. Resuscitative measures give a temporary stay and make successful surgery possible in the severely wounded, but in most cases true release from the consequences of the wound is effected only by surgery. Surgery is not only the goal but is itself a part of resuscitation in the broad sense. Any other view is likely to lead to unfortunate separation between the activities of the "shock team" and those of the surgical team. Care of the wounded man must be continuous and supervision uninterrupted.

Good preparation of the patient for his initial surgery, as well as for the days to come, requires considerate treatment of his pain as well as of a number of psychologic and emotional problems. While lack of understanding in handling these may at the moment be less important than surgical action, a lack of skill here may leave scars as permanently harmful as poor surgery.

PAIN*

The initial assumption of the writer, in common with most physicians

* This has been considered in detail elsewhere. See Beecher, H. K. Pain in Men Wounded in Battle. In press, 1944.

treating the wounded, was that bad wounds are generally associated with bad pain. This was early found to be incorrect. Careful observers in battalion aid stations estimated that only about one-fifth of the freshly wounded had bad pain. Random samplings of groups of patients in the rear supported this view, but it was feared that in these cases too much time had elapsed to permit accurate evaluation, and that possibly the patients were amnesic for the early hours following wounding. Accordingly, when it became possible to study wounded men in the most forward hospitals on the Cassino Front, at the Anzio Beachhead and later in France, this was done, 225 freshly and seriously wounded soldiers were considered in five groups: 50 patients with compound fracture of a long bone, 50 with extensive peripheral soft-tissue wounds, 50 with a penetrating wound of the thorax, 50 with a penetrating wound of the abdomen, and 15 with a penetrated cerebrum. None of the men considered here was in shock at the time of the questioning. (If in shock at entry, questioning was delayed until this had been overcome.) As nearly as possible consecutive cases were considered. Ten of these had to be ruled out of consideration because they were not mentally clear. Nine of these ten had penetrating head wounds. Disregarding for the moment the entire group of head wounds, only one patient of the remaining 201 was not clear mentally and alert.

Of all of the various types of wounds considered, patients with penetrated abdomens have by far the most pain. This may be due to the spilling of blood and intestinal contents into the peritoneal cavity. Infection may have a part in producing the severe pain observed. Only one-quarter of all of the patients on being directly questioned soon after entry in a forward hospital said they were having enough pain to want further pain relief therapy. Three-quarters did not wish such relief, notwithstanding the fact that the most recent morphine had been given several hours before (4.8 to 7.2, average for the various groups). In the paper referred to evidence is presented to show that the difference between the one-quarter of the seriously wounded men that wanted further pain relief therapy and the three-quarters that did not, cannot be explained by differences in dosage or timing of the morphine administered. From the data presented it is clear that morphine is, unfortunately, often administered by rote and not according to need. The use of morphine in the treatment of pain was considered in detail in the other paper and will not be discussed further here.

Thoughtful appraisal of wounded men will show that wound pain is only one cause of suffering. Mental agitation and thirst are factors that may be as important to the patient as pain. The excitement and hyperactivity sometimes encountered in the wounded and ascribed to pain may have their origin not in pain, but occasionally in cerebral anoxia, and more often in mental distress. Repeatedly it was found that a small dose of a barbiturate would provide relief not obtainable by reasonable doses of morphine. Barbiturate sedation offers a real addition to the treatment of the distress of wounded men. Small doses of barbiturates (60 mg sodium

amytal intravenously) and small doses of morphine will frequently accomplish what large doses of either will fail to do satisfactorily (See *loc cit*)

In men in severe shock thirst causes more suffering than wound pain

In terms of planning, care for the mental and emotional problems of the patient falls within the sphere of the chaplain and the psychiatrist. In practice they often have to be dealt with by the medical officer in charge of the preoperative ward, or by the surgeon. Since part of the rôle of chaplain or psychiatrist may have to be assumed at times by the ordinary physician, some of the responsibilities to be encountered will be mentioned

THE PHYSICIAN

His Relationship to the Patient—In the psychologic preparation of the wounded soldier for operation, one must bear in mind that in a high percentage of cases these men are young and their reactions immature. The usual emotional instability of youth has been exaggerated by harrowing experiences. As a result of these the injured have wounds, pain, fear, anxiety. Paternal authority and guidance have been lost and must be assumed by someone. The wounded man seeks it in the chaplain, in the doctor or in his nurse.

Following the confusion of the early hours after wounding, some patients become euphoric. While this is probably more often to be encountered in the early postoperative period, it is sometimes met in the preoperative ward, and may be based upon the overwhelming realization that come what may, the war is suddenly over for the individual. Later the realization that for a longer or shorter time the independent man has become dependent self-reliance is no longer enough, and a profound depression may follow the euphoria. Major Douglas Kelling observed this sequence strikingly in his study of men who had amputations.

The surgeon's first approach to his wounded patient is the most important. He should hope to portray the trusted family physician, being cheerful and self-confident but not casual. This confidence in his own ability is transferred to the patient. (The tactful chaplain will further build up the patient's confidence in the surgeon.) Consultations in the view of the patient are to be avoided. He is likely to think he is worse than the facts justify.

What to tell the wounded patient who asks questions is one of the most difficult problems of the preoperative period. In the case of the correctible wounds—even amputations are in a sense correctible—much can be accomplished. If the need for an amputation is probable but not certain, tell the patient it may be necessary, but that everything possible will be done to save his limb. If the patient will unquestionably have to have an amputation, his general condition permitting, he should be told before operation. But do not leave it there. Point out that many others have had this same experience and have gone on to live normal lives, both maritally (there is much anxiety concerning this) and economically normal.

Failure to tell a patient ahead of time that an amputation, for example, will be necessary may lead to lack of confidence in his future care

Far more difficult problems are the "uncorrectible" lesions—great facial disfiguration, total blindness, loss of genitalia, spinal cord transection. The extent of these wounds is usually not certain before operation and positive statements concerning them usually must await operation. The only help such a patient can be given is confidence that he will get good care and that everything possible will be done, definite answers to his questions cannot be given until later. The proper psychologic handling of this group of patients needs study.

Relationship of the Physician to the Chaplain—The commanding officer or the physician in charge of the patient is often inclined to appraise the value of the chaplain in terms of his (the officer's) personal need for religious support rather than according to the need of the newly wounded man. "There is nothing the chaplain can do that the good physician cannot accomplish." Nonetheless, a fair minority of the seriously wounded are not mentally at ease until they receive spiritual attention. They are lacking and suffer without it. The physician who assumes that he is good at handling such matters often is very bad.*

The physician too infrequently recognizes that a man's spiritual life is a private matter and is too often reluctant to grant that opportunity for private discussion desired by the patient. (Chaplain M I English. This can be compressed to two minutes.)

Dividing the army into two classes, the following generalizations can be made. (a) The enlisted men (in the combat zone at least) are far more religious than expected, where they have grown away from the church, it is usually through carelessness, a passive process. The enlisted man has confidence in the help the chaplain can bring. He wants religious help in a crisis. (b) The officer class presents more education. Members of this group often actively reject religion through an intellectual process. Others are indifferent or "superior" on a "logical" basis. Still others, and many of the best officers are in this group, on recognizing intelligence in the chaplain equal to their own, will act on the assumption that the chaplain knows what he is up to. Since he is not stupid and really believes he has something to offer, the chaplain is permitted to go ahead, although many of these same officers would be hard put to it to give a rational description of what the chaplain could do.

The physician must beware of projecting pastoral care upon the wounded man too abruptly. "Am I that bad, Doc?" The chaplain can stroll in and approach the patients casually, not as though he were arranging a volley ball match and time was short.

* The writer is particularly indebted for good advice on these matters to Captain M I English, a chaplain of wide experience in dealing with the freshly wounded, and to Major Douglas Kelling, Psychiatrist for the 45th Division, also widely experienced with such problems.

THE CHAPLAIN

The successful chaplain, if he is to care well for the wounded, must grasp the fact that the soldier has been torn from his familiar life and thrown into a strange milieu where old standards of conduct are ignored or escaped deliberately. The patient's animal spirits have led to adventures that he knows to be wrong, according to his earlier training. He is wounded and suddenly, unlike the pious old lady who has contemplated death for years, new thoughts of death are thrust upon him with insistence. "As soon as I got wounded I thought 'Damn it, I would have to die without the priest'." He is confused, but mostly he is frightened, and the chaplain as an expert in straightening out misadventures is heartily welcomed. Major Kelling confirms Chaplain English's statement that feelings of guilt are common in the wounded and that discussion of these with the chaplain is helpful to the patient's effort to acquire serenity.*

The presence of the chaplain is especially important to those whose religions embody a ritual of death, chiefly Catholic. "Am I to die?" Priest: "Some do, you might." Contrary to widespread assumption the administration of extreme unction need not alarm. While the point of view is difficult for the writer to accept, both experienced chaplains and experienced psychiatrists insist that it is sometimes desirable to tell a man he is going to die, that such knowledge correctly imparted does good. "My religion is supposed to help me now," and anguished hope gives way to tranquility is the idea. Maybe so, but certainly with the improvements in medicine of recent years, more caution than ever before is necessary if such statements are ever justified.

ADVERSE EXTERNAL CIRCUMSTANCES

In a study by Beecher and Burnett** it was shown that about 25 per cent (of 2853) wounded men arrived at an Evacuation Hospital in need of particular care in resuscitation, with surgical shock either seriously impending or present. Conditions and processes within the patient in part responsible for the poor condition of these patients were referred to above. External circumstances that tend to increase the number of patients arriving at the hospital in poor condition are chiefly these:

* In the experience of the writer, apathy is uncommon in the preoperative ward, sometimes it will be encountered, particularly in those with head wounds, occasionally in men in shock. Anxiety and pain may have led to the need for and use of sedatives and narcotics. Later, memory of this period is often found to be lacking. During convalescence the wise chaplain may be obliged to go over the same ground in discussion several times.

** Beecher, H. K., and Burnett, C. H. Report to the Surgeon, North African Theater of Operations, July, 1944. Field Experience in the Use of Blood and Blood Substitutes (Plasma, Albumin) in the Treatment of Seriously Wounded Men. The Medical Bulletin of the North African Theater of Operations, 2, No. 1, 2, July, 1944.

† Most of these (2296) were at Anzio, where the hospital bore the same relationship to the front as a field hospital.

Exposure—This theater has provided a rich variety of geographic and climatic conditions, desert heat and mountain snow storm, dry country and marshes, high elevation and low. Whether exposure may lead to heat exhaustion or to freezing, it is usually associated with inadequate food and fluid intake and with poor rest. *Delay* in the field or along the evacuation chain lowers the patient's reserves. *Rough handling* may be unavoidable in litter transport down mountain trails, or in prolonged ambulance hauls over rough roads, but it often precipitates shock. *The forward treatment* received in Battalion Aid Stations, Collecting Companies and Clearing Stations will be considered below under various headings. In passing, it may be mentioned that this occasionally accounts for part of the poor condition of casualties as they arrive in the forward hospital. Common errors: Overmedication (morphine), too much plasma or too little, failure to recognize and close an open pneumothorax, failure to check serious hemorrhage, transport of patients with head and pharyngeal wounds on back instead of prone as they should be, failure to protect the patient properly during transport. This ranges all the way from poor splinting of broken bones to inadequate blankets, especially underneath the patient in cold weather.

Chart I shows, for the several types of installations, size, position, representative distance apart, duration of the patient's stay in, and the usual means of his transport along the line of evacuation. In the *Battalion Aid, Collecting* and *Clearing Stations* only the simplest procedures are undertaken, and these with the single aim of making the wounded man transportable—splints and tourniquets are applied, hemorrhage staunched, bandages placed, sucking chest wounds closed, plasma and morphine administered if needed. Nothing is done here that will make the man non-transportable.

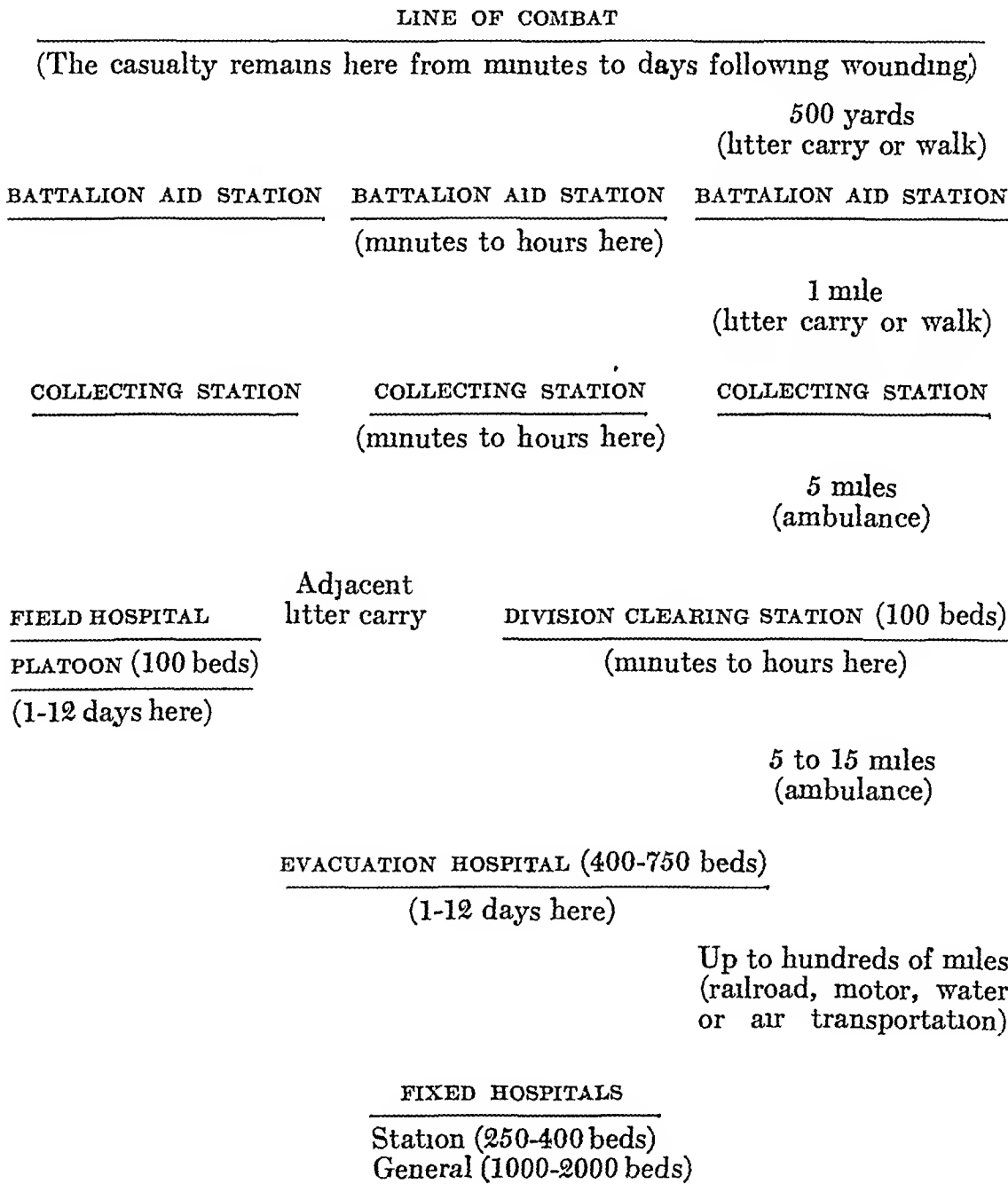
At the Clearing Station the patient's condition is appraised and a decision reached as to whether he must be taken at once next door, to the Field Hospital, for initial emergency surgery, or whether it is probable that he can withstand the further journey of several miles to the Evacuation Hospital where surgery will be carried out. Minor as well as major wounds are treated in the Evacuation Hospital.

Many factors in addition to the patient's immediate condition must influence the decision in the Clearing Station of where to send him: whether the road connecting with the Evacuation Hospital is good or bad, long or short, difficult for blackout driving or not. Also pertinent is the fact that conditions in the Field Hospital are likely to be, because of the very nature of the installation, less satisfactory than in the larger, more completely staffed Evacuation Hospital farther in the rear. This is no commentary on the staff of either installation. For that matter, the mobile auxiliary surgical teams are important in both. With their smaller staff resuscitation may be slower in the Field than in the Evacuation Hospital. Conditions for postoperative care may be poor in the former. For example, the Field Hospital is often far forward, near, and sometimes in front of, the heavy

artillery positions The cannonading makes it difficult for the postoperative patient to get the rest he needs But the well-placed Field Hospital significantly shortens, in comparison with the Evacuation Hospital, the time between wounding and definitive surgery In cases where time or poor condition contraindicate farther transport, the Field Hospital is invaluable

CHART I
THE EVACUATION CHAIN

Representative Distances
and Usual Type of Transport



Eventually, the patients operated upon in the forward area are moved to the rear. As many as possible are returned to duty wherever this is possible along the evacuation chain. If this is out of the question the patient is moved as soon as possible to the fixed installations, the Station and General Hospitals. Here reparative surgery designed to return the patient to duty, to speed healing, to prevent irreparable damage or deformity is carried out. (Since these units serve garrison troops emergency surgery is also undertaken in them.)

MANAGEMENT OF THE PREOPERATIVE AND SHOCK WARDS

During the Tunisian, Sicilian, and Italian campaigns many arrangements for handling preoperative patients were tried out. Many of these plans ended in acute dissatisfaction on all sides. While details of arrangements will (and should) vary from one installation to another, experience has shown that the most satisfactory plans all embody the following:

Personnel for Field Hospitals—The continuous service of one man in charge is important for a period of weeks at least. This individual will be chosen from the internists or the junior surgeons. Indefinite assignment of a surgeon to this post usually leads to discontent and eventually poor care. Twelve-hour stretches of duty are satisfactory, even during heavy drives, but longer periods of work will in two or three days lead to inadequate performance during rush periods. One man must be in charge, but another physician should be trained to cover half of the 24-hour day. At least one nurse or corps man (preferably both) should be on duty at all times to assist the officer in charge.

Personnel for Evacuation Hospitals—Here, again, one man should be in charge, but unlike the Field Hospitals where all admissions deserve "shock" treatment, the majority of patients in the Evacuation Hospitals do not need detailed resuscitative measures (about 25 per cent do). In the Evacuation Hospitals, because of the large volume of patients during drives, two officers should be on duty at a time. One man directs the flow of patients through the preoperative ward to surgery and separates out the patients who are in poor condition. These will be given into the care of an officer who will attend the severely wounded men in poor general condition. At least two corps men and two nurses on duty will be needed at all times.

Relationship of the Surgeon to the Preoperative Ward—A common and serious mistake occurs whenever this ward is used as a kind of valve to regulate the flow of patients to surgery. The optimum time for surgery will be discussed below. There is no known relationship of it to the number of casualties awaiting treatment, presupposed in the flow-meter point of view. The preoperative ward functions satisfactorily only when the surgical chief of service makes frequent visits to it, for he, in collaboration with the officer in charge of the ward, is best qualified to establish priority of operating time. As early as possible cases awaiting operation will be assigned to specific surgical teams. The surgeon, whose patient a given case is, will then, insofar

as it is possible, share in decisions regarding preparation for operation. It is difficult to overemphasize the error of any system which permits one group, as that in the preoperative ward, to carry a patient so far and no farther, then to have his care assumed by a new group, the surgical team, completely unfamiliar with the patient. Good care necessitates continuity of attention.

Routine Procedures in the Preoperative Ward—The care of the badly wounded patient will be described below, but, in general, all clothing is removed at once on admission of the patient. Many^{*} flagrant oversights have their origin in failure to observe this simple direction^{*}. The litter is checked for adequate blankets under as well as over the patient. A complete physical examination is made, and his care planned. If in poor condition, he is sent to the part of the tent set aside for such patients, under the care of the "shock team."

THE PREPARATION OF THE BADLY WOUNDED MAN FOR SURGERY

Surgery imposes a strain, how severe it may be is suggested by the following figures, on the duration of typical operations in the combat zone.

TABLE I
DURATION OF 130 TYPICAL MAJOR OPERATIONS†

Operation	Number of Cases	Average Duration (Minutes)	
		Anesthesia	Induction Time Not Included
Neurosurgery			
Craniotomy (dura opened)	20	109	± 11
Laminectomy	10	122	± 7
Celiotomy	20	117	± 12
Thoracotomy	20	148	± 14
On Extremities			
Vascular injury (involving ligation of large vessel)	20	62	± 5
Compound fracture of femur (includes time to apply spica)	20	83	± 8
Thigh amputation (guillotine)	20	69	± 7

Of the wounds considered here, only those of the extremities could be dealt with surgically in one hour, those of the head, chest or abdomen required two hours. In World War I, operations upon the extremities constituted a higher percentage of the total number than now. The belief that major surgery in war time rarely exceeds one hour may have arisen from that earlier experience, no longer typical.

These data on duration of operation are from the Cassino Front and the Anzio Beachhead, chiefly the latter, where the single large hospital area was near, and, unfortunately, often in the scene of action. Many of the wounded at Anzio were injured on the spot, some in the actual hospital.

^{*} Consider the patient who accidentally discharged his rifle, the bullet passed between his scalp and the inside of the helmet. It followed the curve of the helmet, reversed its direction, and wounded the man in the buttocks.

[†] These data were collected from the cases of many surgeons, all able and experienced. Actual operating time (not including anesthesia induction time) is shown. This material is of interest only as it shows order of magnitude. Consecutive cases were chosen without selection. Standard errors of the means are given to show variation.

area, others on the adjacent road, "Purple Heart Highway" One value of Anzio has been to show that even in the midst of military action, surgical technics of accepted peace-time standards need not be sacrificed (These are jeopardized chiefly by overwork during heavy action)

The operating times indicated here are typical of practice throughout the forward areas in this theater, as such their implications are rather great Little different as they are from those of civil life, they symbolize the revolution that has occurred in surgery since the time of the last war Important factors which make possible such prolonged operating will be discussed later It is clear, from a consideration of these figures, that the patient must be prepared in the preoperative tent to withstand prolonged surgical stress

So far in this discussion, the wounded patient and his passage along the evacuation chain have been described Some indication has been given of the surgical and other stresses the patient must be prepared to meet Hazards of faulty therapy, chiefly of pain, have been considered in some detail Most of the matters that have arisen so far have concerned all patients, the lightly as well as the critically injured man The man who has a slight wound requires little special preparation for surgery The preparation accorded the badly wounded individual may make the difference between survival and death What then are the important elements in this preparation?

APPRAISAL OF THE PATIENT'S CONDITION

As already pointed out, under the condition of the Cassino Front and the Anzio Beachhead for example, one could expect that about 25 per cent of those wounded would fall into the group that is in bad enough condition to require special resuscitative care Attention will be directed to the very badly wounded men, since patients in less serious condition require to a lesser extent the same treatment

Recognition of the man already in poor condition presents few problems The main difficulty comes in early identification of the patient whose condition is deteriorating, recognition of this early enough to check the destroying forces Early recognition here means economy of care, more rapid preparation for surgery (indispensable if congestion in the preoperative ward is to be avoided) and in the end more lives saved

The estimate of which patients will bear watching is usually made on the basis of their immediate appearance Cool extremities and pale skin, with abnormal delay in filling of skin vessels blanched by pressure The blood pressure may or may not be below normal If it is, resuscitative care is obviously urgent The pulse is usually rapid and of rather small volume The appearance of the wound, its extent, the presence of signs of considerable blood loss either internal or external as in blood-soaked clothing, a history of delay in hospital admission, of exposure, of exhaustion, are all points of value Excepting patients with head wounds, the badly injured are nearly

always clear mentally* and can give an accurate account of events since their wounding (although later there may be considerable amnesia for this early period). Great thirst is almost always present and causes much suffering. These conditions give a useful hint of difficulties to come. But most important of all for field use is information concerning the *trend* of the pulse and the *trend* of the blood pressure. The way these swing is of great help in evaluating the patient's condition. A rising pulse rate, a falling blood pressure nearly always forecast immediate trouble, especially if associated with a cool skin, in a man who has been at a comfortable room temperature.

With the fairly general acceptance of the view that the cause of deterioration of the wounded patient's general condition is reduced circulating blood volume, problems of therapy become considerably simplified. This simplification is extended with the further acceptance of the evidence that, excepting the processes that lead to dehydration, fluid lost from the circulation is to be explained by loss at the injury site *alone* (except perhaps shortly before death, when some general increase in capillary permeability may occur as a result of profound anoxia). Therapy falls into three main channels. Treatment of the reduced blood volume, treatment of the local wound, and treatment of pain and mental distress. (See above.)

TREATMENT OF THE LOCAL WOUND AS A PART OF RESUSCITATIVE PROCEDURE

Control of hemorrhage may be accomplished by tying a bleeding vessel, by a pressure-pack or by tourniquet. Tourniquets are useful chiefly as a last resort in the control of hemorrhage, usually in the presence of amputations or near amputations. Since they introduce hazards of ischemia and tissue damage, their use is to be as infrequent as possible. "If a tourniquet is necessary, it is applied as low as possible on a limb. It is not removed until a transfusion of blood or blood substitute is already running into a vein, yet, when it is possible that the limb can be saved, the tourniquet is loosened for a few moments at hourly intervals to avoid tissue damage. In hot surroundings the loosening should be carried out more often. With a hopelessly mangled limb, a tourniquet is applied just below the site of election for amputation. When amputation is performed, the tourniquet is not removed until the extremity has been severed"**.

Splinting provides a means of preventing further tissue damage, further blood loss and helps to prevent pain. Often Thomas splints are applied with the laced shoe in place. Swelling distal to the wound soon produces needless and great pain. (The shoe should be unlaced and slit if it is considered advisable to leave it on.)

* By actual count only one out of 201 badly wounded patients (not in shock) was not clear mentally on arrival in a forward hospital.

** General Recommendation Concerning Shock, prepared at the request of the National Research Council. Submitted July 16, 1942, by Beecher, H. K., Blalock, A., Cope, O., Loeb, R. F., and Warren, S.

Surgery as an indispensable element in resuscitation will be considered below in the discussion of the optimum time for operation. It is clear that at times there can be no resuscitation without surgery, for example, when uncontrollable internal bleeding occurs, sometimes when great fecal contamination of the peritoneum exists, when leakage into and possibly absorption from, large areas of devitalized tissue is taking place. Resuscitation can and should continue during surgery.

FACTORS OTHER THAN FLUID REPLACEMENT FOR CONSIDERATION IN TREATING THE DEFICIENT CIRCULATING BLOOD VOLUME

Just as the available evidence points to reduction in the volume of circulating blood as the chief cause of poor general condition in wounded men, so will correction of this factor go far to restore the patient to good condition. The more rapidly blood is provided (within reasonable limits, to be discussed below), the more rapidly restoration of a condition suitable for operation will be achieved. The considerable change that has occurred in practice, even during the Italian campaign, is suggested by the following figures. In the Field and Evacuation Hospitals below Venafrò and Mignano (Cassino Front) in November and December, 1943, resuscitation of the seriously wounded to the point of operability often required six to eight hours. This contrasts with the more recent experience of Beecher and Burnett (*loc cit*) where very bad-risk patients were prepared for operation and went to surgery in an average of two hours and 20 minutes. The ready availability of whole blood marked an important difference between the two periods. Men who have lost whole blood need blood replacement. Before a detailed discussion of fluid therapy in the wounded is undertaken, a few other matters related to the circulation will be mentioned.

Position of the Patient—Probably the wounded patient's general condition is at the worst it has been at the moment of arrival at the forward hospital, the delay, the handling, the ambulance haul have all contrived to make it so. About a quarter of the poor-risk patients arrive with no measurable blood pressure. Rest and elevation of the foot of the litter (about 12 inches) with the head and heart low, usually are followed by return of perceptible blood pressure, even before fluid therapy can be started. All badly wounded patients should be placed in this position at once upon arrival, excepting some patients with head wounds (chiefly those with adequate blood pressure), some patients with chest wounds (chiefly those whose oxygenation is mechanically impaired by the position), and also excepting patients with pulmonary edema.

Unless the head-down position gives rise to obvious signs of distress, labored respiration or cyanosis, it should be utilized even in patients with chest wounds and with head wounds, as long as the systolic blood pressure is below 8 Mm Hg. When the blood pressure has risen to this level, gradual, slow elevation of the head should be started. As much as 20 to 30

minutes may be needed to get these patients with head and chest wounds up into the semirecumbent position

Gastric Distention—Ideally, all wounded patients should have their stomachs emptied* before being anesthetized in order to avoid the chance of aspiration of gastric contents. A further reason for this practice is to be found in the observation that distention of the stomach is great enough in some wounded men to interfere with the circulation, decided circulatory improvement occurring on evacuation of the stomach contents. The mechanism of this is not clear, possibly the greatly distended stomach interferes with cardiac filling. Vagal reflexes are possibly involved.

Heat—Exposure to cold is not desirable in a wounded man and will affect his condition adversely, so, also, will warming if rapidly carried out. Fluid loss through sweat, increased metabolic needs and dilatation of constricted vascular beds are all possible consequences of the use of heat. The body heat of an injured man should be conserved, rather than heat added. Gradual warming of the chilled man is usually best accomplished by placing him in bed, with plenty of blankets, in a tent at normal room temperature. During even such a gradual warming as this, blood replacement therapy should be in progress. Although the ground was frozen hard and covered with snow in the mountains around Cassino, no occasions were encountered where the addition of heat other than that described above was indicated.†

Vasoconstrictor and "Stimulating" Agents—These are usually of no value in treating the wounded man. In large dose they are contraindicated.

Oxygen Therapy—Whether oxygen therapy is actually of life-saving value in treating wounded men is as unproved as it is in treating pneumonia. It will produce definite signs of improvement (lowered pulse rate, better blood color) and, therefore, appears to be justified on a logical basis.

Much is often made of the fact that cyanosis will not appear when the hemoglobin concentration is about one-third of normal, a rare circumstance, at least in the freshly wounded. In 37 of the worst wounded patients filtered from 2853 wounded men, Beecher and Burnett (loc cit) found on examining them four and one-half hours after wounding (not yet adequate time for complete blood dilution) the hemoglobin averaged 12.3 Gm. The hematocrit

* This is urgent when food or fluids had been taken as recently as two hours or so prior to the wounding or at any time following the wound. The largest tube that will slip down easily should be used. A little judicious moving of this as it goes down will produce vomiting, much to be desired, since only thus can it be certain that the stomach is emptied. Actual washing of the stomach is to be avoided when thoracic or abdominal wounds suggest that perforation of the esophagus or stomach may have occurred.

† One patient was brought in in May, at Anzio, during warm weather, apparently suffering from blast injury with intracranial damage (? hypothalamic area). His rectal temperature was 84° F, and remained at about this level for many hours. Heat was added here, hot water bottles were used, but it was not until the day following injury that his temperature returned to normal.

spread was as follows * 5 were in the 20's, 16 were in the 30's, 8 were in the 40's (only one above 44) and 1 was 50. More important than low hemoglobin in the failure to detect anoxia is failure to look for the signs of oxygen shortage. Moderate cyanosis is too often overlooked as a result of hasty examination and poor light in the preoperative tent.

In the patient whose condition is deteriorating, circulatory changes occur characterized by falling cardiac output and decreasing blood volume. After a time the circulating blood volume reaches a fairly fixed level where it remains, but the cardiac output continues to fall†. These factors lead finally to tissue anoxia, with resulting metabolic change and organic damage and eventually to an irreversible state known as death.

Unquestionably, increase in the oxygen tension in the inspired air is desirable in conditions like these, but how much can be expected of it is open to considerable question. At least until the practical aspect of this question can be better clarified, use of oxygen in field resuscitation should continue. Excepting cases of respiratory obstruction or depression, increase in the volume of the blood and the total quantity of circulating hemoglobin is the chief need. (See below.)

Oxygen is most conveniently administered by nasal tube. (Four or five patients can easily be serviced from a single oxygen tank.) The oxygen is humidified by bubbling through a water column. The well lubricated (12-14 French) catheter should be inserted into the nasopharynx until the patient is observed to swallow a bolus of air, and then the tube withdrawn one-half inch and firmly anchored with adhesive tape to the face. The correct distance for insertion will usually be equal to the distance from the ala of the nose to the ear lobe, less half an inch. Most patients will tolerate a gas flow of four to five liters per minute. Gastric distention is to be avoided. This must be watched for in the unconscious man.

If signs of oxygen shortage are not relieved by the intranasal administration, one can give higher oxygen concentrations. For this a closed system with carbon dioxide absorption, as an anesthesia apparatus can be utilized.

Oxygen therapy should be continued as long as necessary to hold the gains it has effected. (Probably 70 to 100 per cent oxygen should not be administered for more than 12 hours, rarely necessary. If high concentrations continue to be necessary the periods when they are employed should be alternated with 12-hour periods of 50 to 60 per cent oxygen.)

* Hemoglobin, hematocrit (and plasma protein) were determined by the "Copper Sulfate Method of Measuring the Specific Gravities of Whole Blood and Plasma," by Phillips, R. A., Van Slyke, D. D., Dole, V. P., Emerson, K. J., Hamilton, P. B., and Archibald, R. M., for the Committee on Medical Research of the National Research Council, 1943.

† General Recommendations Concerning Shock, 1943 (Revision of Report No. 1 of July 16, 1942), submitted by Bard, P., Blalock, A., Cannon, W. B., Gregersen, M. I., Harkins, H. N., Loeb, R., Long, C. N. H., Richards, D. W., Jr., and Wearn, J. T., for the Committee on Medical Research, National Research Council.

FLUID REPLACEMENT THERAPY

Administration by Mouth vs Parenterally—Discussions of this subject usually begin with a kindly admonition to give fluids by mouth, if the wounded man will tolerate them. The opposite is more nearly in line with good practice: preoperative fluids by mouth are in most cases contraindicated after the patient has reached the hospital where his initial surgery will be carried out. Certainly they are if anesthesia and operation are anticipated in a matter of hours, and almost always this is the case. Gastric emptying time is exceedingly long in the newly wounded man. One can see food and drink regurgitated that were consumed ten hours, or more, previously. It becomes increasingly clear that one of the commonest if not the commonest serious preventable accident to occur on surgical services is aspiration of gastric contents. This may be due to vomiting during anesthesia. Or it may be due to expulsion of gastric contents into the pharynx as a result of surgical manipulation in the upper abdomen, and then followed by quiet aspiration by the deeply anesthetized patient. The accident may be a fatal one. (See preceding section on "Gastric Distention") Naturally, dehydration is to be avoided, or corrected if present. This is done by parenteral injection, chiefly intravenously. A final point: fluids by mouth very often precipitate vomiting, especially in patients with nausea from morphine, so that the net-result of administration of fluids by mouth may actually be a loss of fluid rather than a gain. Patients get considerable comfort but little fluid from a wet sponge to suck and to moisten their dry lips.

Salt and Glucose Solutions—These agents are primarily useful for the correction of dehydration. As "blood substitutes" they are not very effective, and are dangerous. The elevation they produce in blood volume and blood pressure is so transient as to be of little value. The fluid leaks out of the blood stream. In the presence of head injuries the intracranial pressure may be seriously increased by these agents if they are used in large enough volume to produce a significant blood-pressure effect. In the presence of pulmonary damage, or if the heart is working under adverse conditions, they may precipitate pulmonary edema or increase it if it is already present.

During periods of heavy action, when scores, even hundreds, of patients may be awaiting surgery in a single hospital,* the maintenance of an adequate fluid intake in these men becomes a difficult problem. Under such circumstances patients who cannot go to surgery until the next day may be given fluids by mouth. The others may be given normal saline subcutaneously or normal saline and 5 per cent glucose, usually intravenously, but never more than one liter at a time, and in quantities just adequate to keep down definite dehydration.

* At one period during the great Anzio drive more than 300 patients were awaiting operation at one time in the 94th Evacuation Hospital. The situation was the same in the other hospitals of the Beachhead. It was immediately relieved by a shuttle of air evacuation planes to the large hospital base at Naples—40 minutes away by air.

Plasma—The use of plasma as one of the best of the "blood substitutes" is well established. Its use is greatest in the forward installations (Battalion Aid, Collecting and Clearing Stations) where blood transfusion is impossible or its attempt inadvisable, and in the treatment of burns.

Excepting the hemolytic problem in burns, plasma represents the chief need there, for it is the part of the blood lost. Its replacement is indicated. Plasma is a part of definitive therapy. Various rules can be made as to quantity to be used. A common one: Two units of plasma in the first 24 hours for each 10 per cent of the body surface burned, or until important hemoconcentration has been relieved. If laboratory facilities are at hand, give 100 cc of plasma for each point the hematocrit is above a normal of 45. If the plasma proteins are low, 25 per cent should be added to the calculated quantity of plasma needed for every gram the proteins are below six per 100 cc. Better economy is effected in treating burns if the required plasma administration is spaced over 24 hours than crowded into the early hours, for if more is given than needed at one time it is probably lost from the circulation. Secondary shock from burns may occur many hours following the initial injury. The physician in charge must be alert to recognize and treat the anemia that often develops in these cases.

Curiously enough, a fact that is often not adequately appreciated is that plasma, lacking hemoglobin, cannot be, is not, a satisfactory substitute for blood in the wounded man who is seriously bled-out. This state is common in badly wounded men. The great merit of plasma in these cases is that it temporarily sustains the seriously falling blood volume and decreasing cardiac output, it sustains blood pressure at a level compatible with life for a limited time. *Plasma gives more time to get whole blood into the patient.* It should be considered as a stop-gap and not as definitive therapy in patients who have suffered extensive hemorrhage. It has been repeatedly shown in this Theater that plasma, although it will, in many cases, restore for a time adequate blood volume and pressure, in so doing it often gives a false sense of security to those treating the wounded man. *The patient who has been in poor condition because of blood loss, with low blood volume and possibly low hematocrit, will be often seriously endangered if his blood (and effective vascular) volume is increased by plasma without hemoglobin being added.* Such a patient may superficially appear to be prepared for anesthesia and surgery. The blood volume has been restored and the meager quantity of hemoglobin available diluted. The blood pressure has been restored to the level where the already deficient hemoglobin begins to leak out again. A small further loss of hemoglobin from renewed bleeding or during surgery may be critical and sudden disaster occurs. Unfortunately, this has happened many times. *Plasma alone will not adequately prepare the seriously wounded man for surgery.*

One of the most difficult problems is to determine how much plasma should be given in the forward installations. In the badly wounded, 500 cc may be given as the initial dose. In general, plasma should be given only to the extent of elevating the systolic blood pressure to about 85 Mm Hg. The

recumbent patient will not suffer if his skin is warm and of good color when the blood pressure is at this level, and needless loss of hemoglobin will not occur as a consequence of bleeding resulting from pressures that are higher than necessary

While the total volume of plasma to be employed must depend on therapeutic effect and circumstances not possible to treat in generalizations, it can be said that it is rarely necessary to give more than four units of plasma in the four or five hours that often precede hospital admission of the badly wounded individual

After a Field or Evacuation Hospital has been entered, *preparation for operation* will utilize about one unit of plasma to three units of whole blood

Albumin—This fraction of the blood exerts the greatest osmotic pressure of the plasma proteins, 80 per cent of the colloid osmotic pressure of the normal plasma is accounted for by the albumin present Beecher and Burnett (*loc cit*) have given this agent a field trial and have summarized its advantages and disadvantages as they concern military medicine. On the good side is the fact of its small bulk, 25 Gm dispensed in 100 cc solution are said to be roughly equivalent to two units of plasma, when used in the well hydrated patient This was not demonstrated clinically, but possibly the circumstances of the field testing were not adequate to show this difference Albumin, as it is dispensed is ready for instantaneous use No reconstitution is necessary as with plasma It can be administered in one-third to one-half the time needed for plasma It is remarkably stable

Also, to be considered is the following Albumin is expensive in terms of quantity of blood needed to prepare it Its molecule being smaller than that of the globulins, presumably leaks out of the blood stream faster than they do Plasma's natural antibodies have, of course, been eliminated as the albumin is separated out (How desirable these are may be questioned under the present circumstances) The use of albumin is undesirable in the presence of dehydration

Before albumin can be adequately evaluated it needs to be compared in man, with plasma, on the basis of cardiac output and blood volume effects Oddly enough, this has not yet been done so far as can be found Certainly the combat zone is not the place to engage in such studies

In the clinical observations referred to above, albumin was employed in some 200 patients Blood pressure measurements at about ten-minute intervals were followed in 89 patients who received one unit of albumin and in 61 other patients who received one unit of plasma The spread of the initial blood pressures was comparable in the two groups, as were age, sex, hydration, wounds and general condition An average of the data (comparable spreads in both groups) when the initial systolic blood pressure was below 80 Mm Hg (See Table II)

Higher initial blood pressure levels were studied with similar results These data were supplemented by observations of the patient's general condition, peripheral circulation, skin temperature, and pulse rate and quality

Admittedly, all of these data are based upon relatively crude technics of examination clinically, they add up to no demonstrable difference between one unit of plasma and one unit of albumin, theoretically much more powerful

The water administered with the plasma is of course an asset, since the tendency in wounded men is toward dehydration. Concentrated albumin depends for its effect on drawing fluid from the tissues into the blood stream, thus, dehydrating the tissues. In well hydrated patients this is all right, but in dehydrated individuals additional salt and water must be given, usually at the rate of two units of albumin to a liter of normal saline, given intravenously. (Subcutaneous administration of saline or glucose solutions is to be avoided in shock because of the poor rate of absorption as a consequence of the lowered peripheral circulation.)

TABLE II

Factors Considered	Plasma	Albumin
Initial blood pressure (Mm Hg)	49/21 (Av. of 19 cases)	47/22 (Av. of 40 cases)
Maximum blood pressure after 1 unit of blood substitute (Mm Hg)	88/52 (Av. of 15 cases)	83/53 (Av. of 35 cases)
Time to achieve maximum blood pressure (mins)	19 (Av. of 16 cases)	22 (Av. of 34 cases)
Time for fall of blood pressure to begin (mins)	29 (Av. of 9 cases)	33 (Av. of 19 cases)

No significant untoward effects were associated with the use of albumin. In two cases a mild, transient urticaria may have been caused by the agent. Transient moist râles in a patient with a thoracic injury may have been caused by the albumin. (Any sudden increase in blood volume is undesirable in such a case.)

The whole thing boils down to albumin's advantage over plasma being in its small bulk and ready availability. This suggests that it should be useful in Battalion Aid Stations and other difficultly accessible posts especially when transport must be by hand. Conceivably albumin should be of advantage for use with air-borne troops, in ambulance planes, and in submarines, where space and weight are at a premium. Whether in terms of the principles on which army medical supplies are chosen, it is desirable to provide albumin for the exceptional circumstances where it has an advantage over plasma, is beyond the writer's experience.

Blood —(a) Indications for Its Use. The man who has lost large quantities of blood needs blood replacement. Adequate preparation of the seriously wounded man for surgery and support during surgery are impossible without whole blood. This has been demonstrated in probably every preoperative ward and operating room throughout the Tunisian, Sicilian, Italian and Southern French Campaigns. True resuscitation of the wounded requires whole blood. Such statements in no sense minimize the value of plasma. This agent has superbly filled a great need, discussed above.

The best guides in the field for the use of blood are simple, but of great help: the presence of blood-soaked clothing, the nature and extent and duration of the wound, the rate and quality of the pulse, and its trend,

the level of the blood pressure, and its trend, the peripheral circulation as indicated by temperature of the skin and the speed of the response to blanching by pressure, and the color of the mucous membranes

Possibly, too much attention has been given to the fact that on many occasions the blood pressure may be normal yet the patient seriously depleted. Although it may be unreasonable, this has led to a tendency to dismiss the blood pressure as a helpful sign even when it is low—a fatal error, on some occasions. More helpful than the level of the blood pressure, is the direction of its swing—a falling blood pressure, a rising pulse rate, are in most cases an urgent indication of the need for blood.

In the early hours after wounding the kinds of laboratory data available in the field are likely to be deceiving. The hemoglobin, hematocrit and plasma proteins are usually only a little below normal, before blood dilution has taken place. (These factors are, of course, of great help in evaluating the needs of the patient postoperatively, after stabilization has occurred.) Plasma volume information would offer real help. At the present time at least its determination is too time-consuming to be justified for routine use. The simple clinical signs referred to above, rightly interpreted, provide the help needed to gauge the quantity of blood to be used in a given case. Indications for the use of blood are inseparably linked-up with questions of speed of administration and volume to be given, discussed in the following two sections.

(b) Speed of Administration. This depends on how critical the state of the wounded man is. Unquestionably, badly wounded patients need prompt care. In the study of Beecher and Burnett (*loc cit*) the most seriously wounded patients were found to arrive at the hospital at the Anzio Beachhead (short, good roads) more than four and one-half hours after wounding. This suggests that deliberate appraisal of the case is permissible. It is hardly likely that a few minutes more or less on top of the delay already present, in getting the blood or blood substitute into the patient will make any difference. In fairness, however, it must not be overlooked that the handling and ambulance ride immediately preceding hospital entry may have reduced the patient's condition to its poorest. A quarter of the men in this group arrived with no measurable blood pressure. Often only a few minutes of rest in the head-down position was adequate to permit improvement so that measurement of the blood pressure was possible. Action here is governed by rather arbitrary decision based on experience. If the patient's condition is considered to be desperate (systolic blood pressure usually below 60 Mm Hg) he is placed at once in the head-down position (foot of litter elevated about 12 inches) a unit of plasma or albumin started while a transfusion of low titer "O" blood* is obtained. Although patient's blood for later grouping and cross-matching is obtained at the first vena puncture, time is not taken for matching on the occasion of giving the first or at times even the second blood when dealing with the desperately

* Iso-agglutinin titer of 1-64, or less

wounded The first transfusion may sometimes be forced in rapidly by using a bulb (from a blood-pressure apparatus) placed on the blood flask's air inlet tube Rarely this may be necessary for the second transfusion As soon as the blood pressure has begun to rise, efforts to obtain great speed of administration can be relaxed as long as the improvement continues

Subsequent transfusions are usually given more slowly 500 cc blood in half an hour to an hour When the systolic blood pressure has risen to 80 Mm Hg the latter rate is generally adequate So, also, is it for the use of blood prophylactically when fall of blood pressure is to be anticipated, but not actually occurring

For the certain flow of blood in critical periods cannulas should be introduced under direct vision by "cutting down" on the vein In emergencies two transfusions should run simultaneously

(c) Volume of Blood to be Used The young, healthy, organically sound battle casualty will tolerate his wound and the strain of surgery without replacement of all the blood lost It is unlikely that a 3,000-cc hemorrhage is often exceeded Probably a good many lose 1,500 to 2,000 cc of blood Accurate observations on this would be interesting In the study of Beecher and Burnett (*loc cit*) of the most seriously wounded (25 per cent of 2,853) battle casualties it was found that from the time of hospital entry until definitive surgery was completed one unit of plasma or albumin and 870 cc blood were needed on the average before surgery During surgery a further 500 cc was administered to two-thirds of the patients, while the remaining one-third got an additional 1,000 cc blood These patients had come into the hospital (chiefly at Anzio) over fairly short lines of travel from the front (up to ten miles), fairly good roads were available, and the patients arrived as mentioned in four and one-half hours, average, after wounding Certainly, the quantity of blood administered by no means replaced the quantity lost and yet as evidence that these patients were well prepared for surgery the following can be submitted In 2,853 patients who were operated upon, none died during surgery During April and May at the Anzio Beachhead, the hospital death rate in these patients for 1,623 battle casualties was 1.48 per cent Finally, the surgeons were positive in their statements that they considered these patients well prepared for operation

(d) Hazards and Reactions Transfusion of blood, like the transplantation of any tissue, is a complicated process, filled with opportunities for human error With increasing speed and volume of blood used increased strain is placed on the laboratory and those checking and supplying the blood It is also possible that the rapid use of large volumes of nontype specific blood may lead to serious, even fatal reactions Possibly the use of low titer O blood will help to solve this problem Ideally, type-specific blood should be used in all cases, practically this is often not possible

Excluding the accidents when clearly mismatched blood has been given, reactions vary all the way from transient and trivial malaise, chills, fevers and urticarias, to fatal urinary suppression The chills, urticarias, *etc*, have been

shown attributable in most cases to faulty preparation of the apparatus used, either inadequate cleaning or delay beyond two hours in sterilization after cleaning. These reactions even in the field (94th Evacuation Hospital) can be kept below 3 per cent.

Fatal urinary suppression, with death from uremia, has been found in some cases to be associated apparently with kidney damage arising from free hemoglobin or myoglobin deposited there.

Perhaps when large quantities of blood are used, the red cell destruction to be expected results in the liberation of greater quantities of free hemoglobin in the circulation than the body can cope with. Other suggested explanations of the free hemoglobin-containing kidneys—sulfonamide reactions, also "shock kidney"—Exactly what is meant by this last term is not clear, but apparently those who use it refer to a condition in which considerable quantities of hemoglobin or myoglobin are released from traumatized areas. These are absorbed into the blood stream, accumulate in the kidney and appear to impair its function.

One difficulty in determining how much of the kidney problem is to be accounted for by blood and how much by sulfonamide is due to the fact that most patients who have received blood in large quantity have also been liberally dosed with sulfonamides, thus, it has been difficult to separate these two possible causative agents. With the more general use of penicillin, replacing in some cases sulfonamides, the problem of determining responsibility should be easier in the future than it has been in the past. There is the possibility, of course, that sulfonamides, myoglobin, hemoglobin and so on, produce serious kidney damage only in conjunction with some other factors such as low systemic blood pressure.

Two groups at the Anzio Beachhead received identical types of patients, in one the fatal anuria rate was much higher than in the other, yet the use of sulfonamides was not significantly different in the two places. Moreover, since the same types of injury were received in both places, and since several thousand cases were under consideration, the incidence of "crush syndrome" as well as the incidence and duration of low blood pressure was presumably the same in both groups. The group with the higher anuria death rate used considerably more blood and that more rapidly than the other group. It is impossible to say at this time whether or not this is significant. If some as yet unidentified hazard is present in the occasional transfusion and responsible for the anurias, the more transfusions administered, the more anurias one might expect. There is too little evidence at hand to justify much speculation in this direction at present.

(e) Grouping and Cross-matching of Blood. Except for the great emergencies described above, all patient's blood is to be regrouped *and* cross-matched with the donor's blood. It is often stated that this is not possible in practice. The facts are otherwise. Unless great care is exercised in the transfusion of blood the accidents that occur will nullify the value of the procedure. Perhaps in the future fuller information concerning low

titer O blood will reduce the necessity for grouping and cross-matching in the field. At the present time it can be said that there is too little safety in the use of blood unless *both* grouping and cross-matching are carried out. These safety measures need be dispensed with in relatively few cases.

After 1,000 to 1,500 cc of nontype specific blood have been administered to bled-out patients a new sample of the recipient's blood should be obtained for subsequent cross-matching. This process should be repeated after every additional liter of blood is administered.

(f) Alkalinization of the Patient. The evidence on which to base decision concerning this is not as full as one would like. It is sufficient, however, to suggest that patients who receive 1,000 cc of blood or more (as well as those who are on sulfonamides) should be alkalinized.

TIMING OF BLOOD ADMINISTRATION AND OF OPERATION

During periods of heavy military action it must be expected that the blood available may be in short supply, at least its provision will be difficult and economy in its use necessary. The quantities of blood previously mentioned as desirable are half to two-thirds those used and recommended by some experienced officers under the same circumstances. The total quantity of blood needed to see a patient through his operation can be greatly influenced by the timing of its administration. To be specific. When a patient has been extricated from his immediately critical condition and must await operation for a considerable period, elevation of his systolic blood pressure to about 85 Mm Hg is all that is necessary *as long as his color is good and his skin warm*. He can be transfused immediately preceding surgery. In all cases some of the limited blood supply should be saved for use during and immediately following surgery.

In other cases an individual's wound may be such that definitive surgery is a necessary part of his resuscitation. When profuse internal bleeding is occurring it is wasteful of time and of blood to attempt to get the patient's blood pressure up to normal. One should consider himself lucky if a systolic pressure of 80 to 85 Mm Hg can be achieved and then surgery undertaken. This applies as well to other common conditions where full resuscitation is often impossible until the situation has been corrected surgically, for example, where wide fecal contamination of the peritoneum has occurred, where leakage into, and possibly absorption from, devitalized tissue is in progress.

Acceptance of the view that resuscitation can and should continue during surgery will lead to early operation, to be desired in nearly all cases.

It is a matter of considerable surprise to the writer that there has been as much discussion as has taken place in Italy and France concerning the merits of early against late operation in wounded men. Surely, the wound has set several continuing processes in action: there is bleeding and plasma loss from serous surfaces and into traumatized tissues. Contamination leads to progressing infection. With these and other drains upon him, the seriously

wounded patient must have constant external support by way of blood and plasma. If, as a principle, one can say that the smallest quantity of blood and plasma should be used that is compatible with the patient's well-being (until we know more about the cause of the fatal anuria mentioned above, that is an almost obligatory view), then early operation appears desirable on this basis. Unquestionably, delay in operation necessitates the use of larger quantities of blood and plasma to maintain the patient on an even keel than otherwise is the case. A further point is important in this connection. It has been well established in the cases of peritoneal contamination encountered in perforated peptic ulcer that the mortality rate rises sharply with the passage of time. With the grosser tissue contamination met in warfare this is probably also the case. The passage of time is against the patient's good. That early operation is compatible with successful surgery is borne out in the study of 2,853 battle casualties observed on the Cassino and Anzio Fronts, referred to above.

SUMMARY

The enemy has produced the worst wound he could. The immediate physical consequences of the wound and the inseparable mental and emotional problems that arise from it are discussed in terms of what is needed to prepare the wounded man for surgery. Specifically, the distress of the wounded man was found to come from three sources, pain, mental agitation and thirst. Severe pain is usually best treated with morphine, but much that has passed for a response to pain was found to respond to small doses of barbituates. Pain great enough to require further treatment with morphine was found to be surprisingly infrequent (present in only one-fourth of the severely wounded as they arrived at the most forward hospital). A great need was found in the newly-wounded man for the use of small doses of sedatives of the barbiturate type.

The relationship of the wounded man to those around him, especially the physician and the chaplain, is discussed, with a view to preparing the man for his future care.

The effect of adverse external circumstances upon the wounded man and his course along the evacuation chain are discussed with attention being given to details of the organization and application of supportive treatment which must precede the initial surgery. One clue to the extent of the resuscitative measures that must at times be carried out is to be found in the fact that even in the most forward hospitals, the field and the evacuation hospitals, the average duration of operation for craniotomy, laminectomy, celiotomy, and thoracotomy was of the order of two hours or more (not including anesthesia induction time). Even operations upon the extremities averaged more than an hour. The deliberation in the surgery carried out compares with that of peacetime medicine.

Experience has shown that about 25 per cent of battle casualties (under the conditions of study) will require intensive resuscitative measures. The

needs of this desperately wounded group are discussed from three points of view (a) Treatment of the local wound Surgery is an inseparable part of resuscitation in its broad sense On occasion there can be no resuscitation, even temporarily, without surgery (cf internal bleeding, great fecal contamination of the peritoneum, *etc*) In any case resuscitation (blood therapy) should continue during and after surgery (b) Treatment of the depleted circulating blood volume Here, position of the patient, gastric distention as it interferes with the circulation, application of heat and oxygen therapy are all discussed Route of administration of fluids, the rôles in therapy of saline and glucose solutions, of plasma and albumin preparations, and of whole blood are considered in detail In the case of blood administration, problems and hazards concerned with volume and speed of administration are dealt with (c) The treatment of pain and emotional disturbances is discussed

The timing of blood administration and its relationship to the optimum time for surgery are discussed, as, also, is the question of slow against rapid preparation for surgery

GRADUATE SURGICAL TRAINING IN AMERICA*

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FOR THE SELECTION of a philosophical rather than a clinical topic for this address, I make no apologies. In recent years on this occasion we have had so many excellent expositions of clinical subjects that it would be difficult to select one to warrant the imposition upon the time of those courteous enough to listen. The matter of graduate training or graduate education in surgery is one which has engaged the interest of the speaker for many years. In the light of present conditions it should properly engage the interest of all of us. I propose, therefore, to discuss this subject, particularly in relation to American surgery. It follows, that in order to do this intelligently one must first review the past, consider the present and venture a few suggestions regarding the future.

The beginning of the twentieth century saw surgery in America in the hands of "doctors who operated." These men were mostly physicians who, through interest and manual dexterity, were recognized by the public and their fellow practitioners as surgeons. For the most part, these men continued to engage in the general practice of medicine, and it is doubtful whether anyone really confined his work to surgery. It was the usual thing for the so-called surgeon to attend medical cases, deliver babies and to treat diseases of the eye, ear, nose, throat and skin. In general, the surgeon was merely a superior breed of doctor. He acquired proficiency either by long hours spent in the dissecting room or the dead house. In the former he learned anatomy, and in the latter became familiar with the gross appearance of diseased organs and tissues. This knowledge he applied to his practice. Many of the pioneers in American surgery followed this path to glory. In our own city the elder Gross and Agnew may be cited as examples. Later the period of "study abroad" appeared on the horizon, and of this probably the least said the better. Suffice it to say that the recent graduate, or the practitioner of better than average means took a year off and went to Vienna where he acquired or improved a taste for beer, sent postcards to the folks at home, and eventually returned to become a specialist, by announcement. In this country a number of short, or so-called polyclinic courses were given in various medical centers. To these came doctors for surcease from the rigors of practice and a little fun in the big cities. Neither "study abroad" or the polyclinic course had any significant influence on the progress of surgery in this country.

The American College of Surgeons, founded in 1913, represented the first attempt to set up a standard by which true specialization in surgery might be recognized. By this time there was a not inconsiderable number of surgeons

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who, through long apprenticeship and clinical experience, had attained the status of the specialist. In its earlier days the College attempted to formulate requirements for recognition of surgeons. Later it extended its activities to provide the facilities by means of which these requirements might be met. One need only consider the size of the country where surgery was being done in communities varying in population from the metropolitan city to the village to realize the enormity of the task undertaken by this organization. Those who have been inclined to criticize and belittle the work of the College should bear these facts in mind. That a uniform standard, applicable alike to the metropolis and the village, was impossible of achievement should not be allowed to negate the splendid contributions of the College to the cause of American surgery. It follows as inevitable that some unworthy ones were admitted to Fellowship.

Requirements for admission to Fellowship in the College have been gradually raised over a period of years. The present requirements are three years of hospital service, two of which must be spent in a surgical service acceptable to the College. In addition, it is stated that the candidate must restrict himself to "study, diagnosis and operative work in surgery," but in the same section the statement appears that "the minimum participation of specialization may vary according to the character and size of the community in which the applicant resides." Furthermore, it is stated that each application shall be judged upon its individual merits.

In 1915, the first formal Fellowships in general surgery were instituted at the Mayo Clinic, and to date approximately 825 men have completed this training. In 1916, the Graduate School of Medicine of the University of Pennsylvania was organized and offered the first full-time academic course in surgery, which included work in the basic sciences and led to a higher degree. The residency system, originated at the Johns Hopkins Hospital by Osler probably constitutes America's outstanding contribution to training in surgery. To date 41 men have completed the chief residency in surgery at this institution. Of the residency system, more later.

In 1916 the first Specialty Board was constituted in Ophthalmology. The organization of other similar constituted Boards for other specialties followed. The American Board of Surgery was constituted in 1937, and held its first examination the following year. To date 1279 have been certified by examination (1277 men and 2 women). To qualify for examination before this Board the candidate must present satisfactory evidence of at least five years of training following completion of a minimum internship of one year. This five-year period must be devoted exclusively to training and must include work in the basic sciences of Anatomy, Physiology, Pathology, Chemistry and Bacteriology. Three of the five years must be devoted to general surgery, not more than six months' credit is allowed for work in any one of the previously mentioned basic sciences, or to such specialties as Gynecology, Urology, Orthopedics, *etc*. Recognizing the value of a sound basis of general diagnosis and internal medicine, the Board has accepted a full year of residency

in medicine for credit toward the five years' training. In addition, evidence of adequate operative experience is required. The examination itself is comprehensive and rather difficult. From the foregoing it will be obvious that many men who can qualify for Fellowship in the College are unable to qualify for certification by the Board. The most frequent cause of rejection of applicants is inadequate training, failure to limit to surgery ranks second. A limited number of applicants are rejected on ethical grounds, for example, the practice of division of fees.

This brief summary of the past brings us to a consideration of the present status of graduate education or training in surgery.

Today the recent graduate who desires to become a surgeon has several paths open to him. Regardless of the plan the trainee elects, the objectives are the same. He must review the basic sciences with reference to their application to surgery. He will have forgotten much of his anatomy if he graduated from a school in which anatomy is still taught. If he comes from any one of the majority of the leading schools where anatomy in recent years has been compressed into periods of from three to six months, he will not have forgotten it for the simple reason that he has never learned it. With regard to physiology likewise, the average graduate will recall that most of his undergraduate hours in this important subject were devoted to the making of nerve muscle preparations and recording the responses of the same on a smoked drum. As to the more important matters of the physiology of nutrition, of liver function *etc.*, he will have at best a very hazy conception. His training in pathology will be somewhat better, but it will probably be some time since he has looked at a slide under the microscope. The failure to correlate these basic sciences with clinical medicine and surgery is largely due to the fact that these departments are for the most part headed by Ph.D.'s who regard the instruction of undergraduate medical students as a penance which must be fulfilled in order to enjoy the facilities for research in pure science. To put all this into the language of the street "The tail wags the dog."

In addition to building a foundation upon the basic sciences, the candidate must have opportunity to adequately study surgical patients before operation in order to foresee what may happen to them after operation, and provide protection against such eventualities. Above all, he must have opportunity and time to read and to think, and to discuss his problems day by day as they arise with an older, more experienced and understanding preceptor.

The Apprentice System—This plan, under which most of the senior Fellows of this Academy were brought up, still has a definite place in the education and training of the surgeon, although in recent years it has become fashionable to refer to the apprentice system with something between reluctant tolerance and ill disguised contempt. For many an aspirant to surgical training, however, it offers the only opportunity. Under this system the tyro associates himself with an established surgeon, assists him at the operating table, takes charge of the pre- and postoperative care of patients,

is gradually eased into greater responsibilities and, finally, is permitted to operate independently. During this apprenticeship, unless his chief pays him a salary, which is uncommon, the trainee is hard pressed to earn a living, and in spite of good intentions too often finds it necessary to engage in general practice "on the side." Unfortunately, the general practice often takes precedence over surgical training. This does not infer that by means of the surgical apprenticeship combined with general practice he may not become a competent operator, but he rarely is able to give sufficient time to surgery to become a well-rounded surgeon. Training of this type, in which the trainee conducts a general practice while acquiring surgical experience, is not acceptable for credit by the American Board of Surgery, and is responsible for the rejection of a considerable number of applicants for examination by that Board. Many of these men may qualify for Fellowship in the American College of Surgeons.

The Residency—Previous reference to this system has been made. As stated it had its beginnings at Johns Hopkins Hospital. As originally set-up in that institution a young physician spent an indefinite number of years living in the hospital in order to complete his training. With the Hopkins' plan as a working model, the residency system has been extended to practically all teaching hospitals and to many not connected directly with teaching institutions. The properly set-up residency is probably the best system by which a young physician may receive adequate training in surgery. The widest differences, however, exist in these residencies. The Council on Medical Education and Hospitals of the American Medical Association, and the American College of Surgeons, maintain services which inspect and approve institutions for such residencies. In their most recent publications the former has approved 275 and the latter 162. Each has set-up standards for approval. On paper these are excellent. In actuality, some of the approved residencies are nothing more than internships in which the trainee is shockingly exploited and spends his time in routine drudgery, failing completely to receive real instruction, and has neither opportunity nor time to think—both of which are essential. It is inevitable that the best residencies are to be found in teaching hospitals. It by no means follows that good residencies are limited to such institutions. It is not necessary that a residency be taken in a teaching hospital, but it is essential that the director of the residency be a teacher. One of the greatest difficulties in the nonteaching hospital is the meeting of the requirement pertaining to instruction in the basic sciences. Both of the approving bodies previously referred to require such facilities, as does also the American Board of Surgery. Provision for instruction in Anatomy, Pathology, Bacteriology and Surgical Physiology is essential. In a hospital connected with a medical school this is a simple matter. In the well conducted nonteaching hospital adequate instruction may usually be provided in Pathology and Bacteriology. Anatomy and Physiology present difficulties, but not necessarily insurmountable ones. In New York City, for example certain hospitals have negotiated an agreement with Columbia University

whereby a resident desiring to meet the basic science requirements of a Specialty Board may obtain such instruction without cost, other than the payment of a nominal matriculation fee. This plan should be extended to other teaching centers throughout the country. It is already being applied, in part, in two other localities.

Formal full-time graduate instruction in a University School offers a solution to some of the problems which have proved difficult in the apprenticeship and the residency. The University of Pennsylvania was the first to offer such instruction. Organized in 1916, the first group of student physicians was received in 1919. Under this plan a full academic year is devoted to a comprehensive review of the basic sciences of Anatomy, Physiology, Pathology and Chemistry, together with systematic courses in operative surgery on the cadaver and on living animals. In the latter, the major effort is concentrated upon the mastery of fundamental surgical principles, such as prevention and management of shock, control of hemorrhage, prevention of infection, wound healing, *etc*, rather than upon cutting and sewing—things which, after all, are the easiest that the surgeon is called upon to master. In conjunction with the foregoing, the student physician is afforded ample opportunity to observe the conduct of operations in the many clinics of Philadelphia, and in the University Hospitals, to maintain close contact with the pre- and postoperative care of patients.

From the beginning, the Graduate School has emphasized the fact that it did not attempt to make a surgeon in one academic year, but it has maintained that with such an academic year behind him, the student physician is placed in a position to become a surgeon through additional clinical training. Those of us who, for many years, have participated in this program of graduate education feel that it has a definite place in the making of surgeons and offers a solution to the conspicuous shortcomings of the purely apprentice type of training. That this feeling is shared by many is evidenced by a steadily increasing number of well qualified applicants each year. The Graduate School encourages the continuation of training by placing those who complete the basic year in acceptable residencies. After the satisfactory completion of two years in such a residency the trainee may, upon presentation of an approved thesis, be awarded the degree of Master of Science in Surgery, or upon the completion of an additional two years, that of Doctor of Science. The American Board of Surgery gives full credit for time spent in this program.

The Graduate School should take a more active part in securing clinical opportunities for those who complete the basic year than it has heretofore. Failure to do this constitutes one of the definite shortcomings which must be remedied.

These three plans—the apprenticeship, the residency and the graduate school—are the paths by which the surgical neophyte may arrive. Most men undertaking training under any of these have as their objective certification by the American Board. In the light of experience acquired through partici-

pation in the examinations of this Board, and in the evaluation of candidates for examination, certain conclusions regarding the merits and shortcomings of the three may be drawn. For the apprenticeship plan, on the credit side one finds that it offers probably the maximum of actual operative experience and tends to the development of the ability to think and act quickly. It also offers greater opportunity for a young man to acquire a surgical practice and, hence, financial security at an earlier date. On the debit side, it is unquestionably true that the surgeon trained today under the apprenticeship plan is likely to know much more of the "how" than of the "why" of what he does. If apprenticed to a typical "cutter and sewer" he may see and not perceive, and may accumulate experience which consists, for the most part, of the repetition of mistakes. These men are prone to the early development of cerebral rigidity, characterized by resistance to progress or change, and an attitude of intolerance and criticism toward those whose horizons are not fixed.

The residency, if it be well organized, is without doubt the best form of training. The residency, unlike the apprenticeship is an educational discipline. The resident advances gradually along a well defined path. He is given instruction in the basic sciences as applied to surgery. He is encouraged, or rather compelled, to use his powers of observation in the study of his patients. He must stand up and be counted when it comes to errors in diagnosis, technic or judgment. In the final phase of his training he is given an opportunity to operate independently. He is encouraged to think his problems through and is given constant help and encouragement in their solution. Above all, if the residency is under the direction of a proper preceptor, the candidate can not but profit through precept and example of the one who stands to him *in loco parentis chirurgiae*.

The residency is, however, not without its shortcomings. The question of the optimum length of time which should be so spent has not been answered to the satisfaction of everyone. The original residencies at the Johns Hopkins were of indeterminate duration, and this, in itself, is not altogether desirable. In time the resident who stays too long develops a cloister complex. He becomes so accustomed to having immediately at hand everything to work with, and someone to whom he may always appeal for help in extremity, that he inevitably loses some of the self-reliance which is part of the essential armamentarium of every surgeon who is confronted with surgical actualities. He may remain so long in his institution that his value to the surgically sick public may be permanently impaired. Again, these long term residents sometimes become sidetracked through concentration on some restricted phase of surgery. This is not by way of criticism of the magnificent work that has been done by many such individuals, but it is, nevertheless, a fact that a vast amount of effort, primarily intended to qualify a man to take care of surgical patients has been wasted. For example, it is completely unnecessary to spend five years in a surgical residency in order to make contributions to the literature of the bacteriology of surgical infections. Such a man has not

only wasted his own time but has also prevented another, possibly equally or even superiorly qualified, from becoming a surgeon. In the examination for certification of many men, the product of the protracted residency, the writer has been impressed with the shocking lack of knowledge of certain matters with which all clinical surgeons should be familiar.

Fellowship in the great clinics, of which there are a number in this country, offers certain things which the residency of indeterminate duration lacks. A more realistic attitude toward the practice of surgery is cultivated and the necessity of getting things done is impressed upon the trainee. He acquires a lively sense of responsibility with regard to results. He probably has a better opportunity to become familiar with the correlation of general surgery with the surgical specialties and internal medicine. He definitely does not have the opportunity to operate independently, nor in some instances even to act as first assistant at the operating table. This form of training is an excellent educational discipline, but before the trainee may take his place and receive the stamp of approval as one qualified to undertake unsupervised the complete responsibilities of the surgeon, he must supplement his Fellowship with some sort of apprenticeship or precepteeship. Here, as in the product of the protracted residency, there is a tendency toward intolerance of his less fortunate brethren of the common herd.

The student physician who completes the basic year in a Graduate School must supplement this year by further clinical training if he is to qualify before his examining board. There are, however, each year some who take the basic course in order to fill some hiatus in their training. Many of these have had considerable clinical experience, but feel that they lack knowledge of the basic sciences as applied to surgery. Only occasionally in recent years have those come who desired refresher courses and the policy of our own institution in normal times has been to discourage them. The Graduate School, in spite of all the criticism leveled at it, has served a useful purpose in the past and will continue to do so in the future. It offers to a significant group of qualified student physicians facilities for formal instruction which cannot be obtained elsewhere.

Having considered the past and the present in graduate training in surgery, we now come to the future.

Any discussion of the future must deal with two separate and distinct phases of the problem. First, the immediate post-war period and, finally, the long range aspect. The induction into the armed services of practically all able-bodied physicians of trainee age brought graduate education in the usual sense to an abrupt halt. Those who had partially completed their training were forced to interrupt it. Those who might, in the normal course of events, have begun training were forced to postpone it. Thus, the annual supply of trained young surgeons ceased. A whole medical generation may be conceivably required to remedy the situation thus created. The so-called residency of nine months, which the War Manpower Commission has been graciously pleased to permit, is probably worse than nothing, since it will create a group

of inadequately trained men who will consider themselves as superior to other less fortunate contemporaries who were placed on active duty at the end of a nine months' internship. Of these, it may be truly said that a little knowledge is a dangerous thing. The product of the nine months' residency will have no significant effect on the general problem of developing surgeons in this country. It is a stop-gap to permit the more efficient care of patients—nothing more or less.

In the period immediately following the cessation of hostilities our first consideration should be for those whose formal training was interrupted by entry into the services. To them should be given the opportunity of completing their training should they desire to do so. Replies to questionnaires sent to physicians in the armed forces indicate that a majority of medical officers desire some sort of graduate education upon discharge from the services. The "G. I. Bill of Rights" will make this available to all who desire it. We must, therefore, prepare ourselves to provide proper facilities for it. If in any way possible those whose training was interrupted should be allowed and encouraged to return to the clinics from which they came. The problem of evaluating their military service for credit before the Boards is a real one. In all fairness, it must be admitted that much of the experience incident to service will be of little permanent value. The surgery of war is, at best, rough and ready surgery and is largely confined to the surgery of trauma. Even in this restricted field the young surgeon has scant opportunity of following his patients or of knowing what eventually becomes of them. He, therefore, does not learn to know what to expect from what he does. In other words, there is but little chance to acquire surgical judgment. However worthy the service, or patriotic the motive, military service inevitably will occupy a minor place in surgical education. The American Board of Surgery, after careful consideration of every aspect of this problem, has allowed one year of training credit for the first year of service with the armed forces, regardless of how that year is spent. This is a gesture recognizing the sacrifice that the young doctor has made and not an admission that a year in the Army or Navy is the equivalent of a year of training under normal conditions. Beyond this first year credit will depend upon the actual type of service engaged in. If a candidate is assigned to the surgical service of a regularly constituted military hospital, credit may be allowed upon the submission of an acceptable record of service. The Board has not lowered or modified in any way the other requirements for admission to examination, nor has there been any change in the character of the examination itself. To do either would be manifestly unfair to those who have qualified in the past and who will qualify in the future.

It is quite possible that the American College of Surgeons may change its method of admission to Fellowship. A special committee appointed to make a study of the subject has already submitted a preliminary report. The following citations from this report are here given by permission of the chairman of the committee, Dr. Frederick Collier. The question has

been raised "Could not the American College of Surgeons conduct an examination in the basic principles of surgery, replacing Part I of the examination now given by many boards?" This would, in addition, serve as an initial test for those aspiring to Fellowship in the College. Following this examination, and after further training, those who passed the initial examination would later take the examinations given by the various Boards of the Surgical Specialties. After having passed his particular Board, the candidate would become eligible for Fellowship in the College. This plan would take care of all men intending to limit their work, but it would not take care of a large group of men practising in small towns and who, while doing good surgery, either are unable or unwilling to confine their practice to surgery. The report offers the suggestion that the character of Junior Fellowship might be changed. This might be reserved for those who have passed the initial examination, but subsequently failed to limit their practice. Since the title of Junior Fellow would be for a limited number of years, and be continued only during good behavior, this group would be encouraged to secure further training and to otherwise meet the requirements for certification by a Board and for Senior Fellowship in the American College of Surgeons. Such a plan would bridge the years between the present and the time when enough men with adequate training will be available to every community.

For those who had come within one year of completing their training, the problem is simple. For those who have had less, it will be difficult in direct proportion. For those who would have commenced their training but for the war, it will be most difficult of all. Many of this latter group will be, for one reason or another, permanently lost to surgery. Regardless of the subdivision into which they may fall, each and everyone of these men deserves well of his profession, as he deserves well of his country, and it is the obligation of all of us who are concerned to see to it that he is not let down. This will be no simple obligation to fulfill. With each year of the war the number of men for whom training facilities must be provided after the war will increase. Even before the war there were not enough places where men qualified to undergo training in surgery could obtain it. Thus, the necessity for some long-range plan becomes obvious and naturally merges with the immediate post war problem.

Various estimates of the qualified surgeons required annually to replace those deceased, superannuated, or retired for other reasons, place the figure in round numbers from 200 upwards. These figures are not completely reliable since the methods of arriving at the annual requirements differ considerably. In order to supply 200 completely trained surgeons each year, approximately 1,000 would have to be in training if a steady supply is to be maintained. If more than 200 new surgeons are required annually, the number in training would have to be proportionately greater.

The need for increased training facilities can be met only by the creation of more residencies. There is in the country today a shocking waste of opportunity in this respect. As stated elsewhere, there are countless hospitals

where the men and material are available for setting up excellent training programs if sufficient interest can be aroused. One often hears, when suggesting that such a plan be initiated, that it is too much trouble. Such people require education and should be made to see their responsibilities. No chief of a surgical service who has experienced the satisfaction which attends a well organized residency would ever voluntarily return to a system whereby he depends upon the services of an intern and a part-time apprentice. It is to be regretted that an occasional hospital superintendent questions in terms of dollars and cents the value of a resident to the hospital. These too must be shown the light.

I have attempted in this communication to discuss the past and the present in Graduate Surgical Training in America. Certain aspects of the future have been touched upon. Certain it is that the responsibility for keeping the torch of surgical progress burning will reside for many years to come in the hands of American surgeons. Let us dedicate our best efforts to the end that we may prove worthy of this responsibility.

LOCAL FLUID LOSS, NERVE STIMULI AND TOXINS IN THE CAUSATION OF SHOCK*

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THE RECENT EXPERIENCES OF SURGEONS in both civilian and military practice^{1, 2} confirm the experimental evidence submitted during the past fifteen years that local loss of circulating fluid is by far the most outstanding cause of traumatic shock in persons in relatively good general condition at the time of injury or operation. No better proof could be offered than the striking improvement in the prevention and treatment of shock that has been obtained by very adequate and timely transfusions of blood and plasma before, during and after operative care.

Nervous and toxic factors have been investigated, but so far little information has been acquired that is of service in the treatment of the shocked patient. Working on the theory that nerve stimuli from the seat of injury or operation produce shock, attempts were made by surgeons to prevent its occurrence by the blockage of nerve impulses. This was carried out by the injection of a local anesthetic into the field of operation or into nerve trunks, either as a supplement to general anesthesia, in pursuance of the anoci-association technic of Crile,³ or as the sole anesthetic agent. After years of very extensive trial this method of preventing shock has met with so little success that its use has been practically abandoned. Local infiltration or block anesthesia is used whenever feasible for operation where shock is threatened or present, but this is done because the general toxic effects are usually less than those of general anesthesia and not because of the possible shock-preventing benefits of nerve block. The general toxic effects of spinal anesthesia, except when large doses are given for high anesthesia, are also usually less than those of deep general anesthesia. This is especially true of continuous spinal anesthesia when used in prolonged abdominal operations where good relaxation of the abdominal wall is essential. However, where marked impairment of the circulation from any cause is present before operation, the frequent additional lowering of blood pressure and disturbance of respiration produced by spinal anesthesia contraindicates its use, as the condition may be seriously augmented.⁴

Swingle, and coworkers,⁵ have recently concluded from limb trauma experiments performed on dogs, that a flow of nociceptive nerve stimuli from the traumatized area played an important part in the production of the shock that ensued. It was reported by them that when an amount of trauma somewhat greater than that required to produce shock and death within a few hours in control experiments was administered in the presence of procaine

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spinal anesthesia and the anesthesia maintained for three to four hours, the incidence and severity of shock was greatly reduced. In 12 such experiments ten of the dogs showed none of the characteristic symptoms of shock, and recovered. They state "The evidence was quite convincing that prolonged spinal anesthesia effectively prevents shock resulting from muscle trauma of the type described." And, again "The evidence indicates that a flow of nociceptive stimuli from the traumatized regions, unless prevented by spinal anesthesia or a local block, is an important contributing factor in the initiation of the shock state which follows the type of muscle trauma employed." Also "The nervous factor taken in conjunction with the loss of blood into the injured area almost invariably produces shock, but it is improbable that either factor considered apart from the other is sufficient to induce a fatal outcome in the type of trauma employed."

They made use of local block (1) by injecting a 2 per cent to 4 per cent procaine solution either directly into or about the major nerve trunks or diffusely into the muscles of the limbs, and (2) by applying tight constrictors to both thighs. They report that while considerable success was obtained by these methods, they did not give a protection against shock as complete as that afforded by spinal anesthesia. However, because they found these methods partially successful and spinal anesthesia almost wholly so, they conclude that this "seems good evidence for the existence of a nervous factor in this type of shock."

All of their dogs were anesthetized with ether, and, when spinal anesthesia was used, a 2 per cent procaine solution was injected at the level of L-3-4 in amounts varying from 18 to 30 cc, according to the weight of the animal. This reduced the blood pressure to an average of 75 Mm of Hg. Both hind limbs were then traumatized with a rawhide mallet, after which the ether was removed and the spinal anesthesia continued for three to four hours by two or three subsequent injections of procaine.

They considered the criticism that since the blood pressure under spinal anesthesia was low, the trauma would produce less extensive hemorrhage and, therefore, less tendency to shock from local fluid loss. However, since the trauma was greater than in the control animals and since some protection was afforded by nerve block from pressure by a tourniquet or by procaine infiltration, which caused no fall in blood pressure before trauma, they felt that this criticism had been met. Pooling of blood was found in the traumatized tissues, but no measurement of the amount of local fluid loss was made.

In a subsequent publication⁶ the same authors reported that in a very large majority of cases neither cutting of the major nerves to the hind limbs nor complete section of the spinal cord at the level of T-13/L-1 prevented the development of fatal shock after the same kind of limb trauma had been applied. The findings are paradoxical in terms of the previous report of these authors, in which they stated that procaine nerve block or spinal anesthesia is an important protection against shock by eliminating nociceptive

stimuli from the traumatized hind limbs. They also reported that if only the ventromesial portion of the cord with its descending tracts was preserved, the animals were protected against limb trauma shock of the type described, that cutting this area might sensitize to shock by causing vasodilatation and excess pooling of blood in the traumatized region distal to the level of the cut.

Spinal anesthesia produces temporary blockage not only of the sensory fibers but also of all other fibers of the roots of the spinal cord that are sufficiently exposed to the anesthetic agent. Blockage of the sensory fibers arrests not only sensation but presumably nociceptive stimuli. Blockage of the vasomotor fibers is generally recognized as the principal cause of the fall in blood pressure. Blockage of the motor fibers, by paralyzing the voluntary muscles, contributes to the fall in blood pressure by diminution of intra-abdominal tension, by interference with respiration and, according to some authors,⁷ by removal of extravascular support of the capillaries, venules and veins thus, causing a pooling of blood in the involved areas. Blockage of specific afferent pressor and depressor fibers, which are known to exist,⁸ might be expected to have little effect on blood pressure since the action of each type of fiber is antagonistic to the other and their effects are neutralized when both are removed.

If some of the findings and interpretations reported by Swingle, and his coworkers, are valid, they call for attempts to extend the field of spinal anesthesia and renewed efforts on the part of surgeons to prevent shock by the blockage of nerve impulses from the field of operation or injury by the use of local anesthetics. In a search for more evidence on this subject, an effort was made to determine how much of the reported protection against limb trauma shock afforded by spinal anesthesia was due to blockage of sensory nerves preventing the flow of presumable nociceptive stimuli from the traumatized field and how much was due to blockage of vasomotor and motor nerves with resultant temporary fall in blood pressure reducing the amount of hemorrhage. Experiments were conducted on 38 dogs, divided into three main groups. The trauma was limited to the right hind limb and the local fluid loss was determined by comparison of the weights of the hindquarters, using the bisection technic of Blalock.

In Group 1, control experiments, the trauma was applied with the nerve pathways of the hind limbs intact and the blood pressure at normal levels. In Group 2 the trauma was applied with the nerve pathways of the hind limbs and much of the trunk blocked and the blood pressure lowered by spinal anesthesia. In Group 3 the trauma was applied with the nerve pathways intact, but with the blood pressure in the right hind limb lowered by ligation of the right iliac artery and one or more proximal branches of the femoral artery. Thus, it was possible to test the relative rôles of nociceptive stimuli and local fluid loss in the production of limb trauma shock in animals both with and without preliminary blockage of the nerve pathways and with and without preliminary lowering of the blood pressure of the traumatized region.

EXPERIMENTAL TECHNICS

The hair of all dogs was clipped from both hind limbs and the torso up to the level of T-13. The animals were then restrained on their backs and anesthetized with ether until the completion of traumatization. The initial and subsequent blood pressure readings were made by punctures of the left femoral artery and the blood samples were taken at the same time when needed. Red count, hemoglobin and hematocrit determinations were made on samples taken before etherization, 15 to 30 minutes after traumatization and at varying intervals thereafter, depending upon the type of experiment and the length of survival. Trauma was applied with an 800 Gm padded hammer to all faces of the right thigh and upper leg, approximately three-quarters of which was to the anterior surfaces. Blows were so moderated that skin, bones and femoral artery and vein were not broken, as verified by necropsy.

The results in several hundred limb trauma experiments in this laboratory during the past 18 years have shown that there may be considerable variation in the amount of local fluid loss when a uniform technic of hammering is attempted. This is due in part to the human error of varying from day to day the severity and distribution of the trauma, in part to chance injury of larger vessels producing more extensive hemorrhage in some experiments, and in part to anatomic variations in blood supply. In this study, when blows were unintentionally severe enough to tear the femoral artery (one case) or to break the femur (two cases), the hemorrhage was relatively great, shock and death ensued and the experiments were excluded from the three groups.

In those experiments in which the animals were sacrificed termination was effected by ether. Aseptic technic was employed in all experiments in which the animals were returned to their cages and given the opportunity to survive. The increase in weight of the traumatized over the nontraumatized side is recorded in grams, and is also expressed in per cent of the blood volume, which was estimated at 10 per cent of the body weight.⁹

EXPERIMENTAL RESULTS]

Group 1 —The results are shown in Table I. In these control experiments, with the blood pressures starting at normal levels, the trauma applied averaged 20 blows per Kg of body weight. The limb swelled rapidly as it was hammered, and the swelling was extensive in all cases by the time the blood pressure had been definitely reduced to a shock level. The number of blows was varied in two cases to accord with the amount of limb swelling and embarrassment to the circulation. When the blood pressure was read 15 minutes after completion of trauma the pulse was weak and accelerated and the respirations somewhat embarrassed. The pressures declined steadily until death took place.

Careful observation revealed that by far the greatest part of the swelling took place during the hammering, which indicated an early, rapid loss of blood into the field of trauma. Further swelling was most marked during the

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first five to ten minutes following trauma, after which the progress was slow and an increase in the spread to the abdominal wall above the limb occurred. This quick retardation of swelling was taken as evidence of early sealing off of the opened vessels under the favorable condition of lowered blood pressure from blood loss. The changes in red blood count, hematocrit and hemoglobin indicated a very slight to moderate blood dilution.

TABLE I
FLUID LOSS IN RIGHT HIND LIMB TRAUMA IN CONTROL DOGS DYING IN SHOCK FROM TRAUMA

Exp No	Wgt Kg	Control Blood Pressure mm Hg	Amount of Trauma Blows/Kg	B P 10 Min After Trauma mm Hg	Survival After Start of Trauma Hrs	Fluid Loss Into Traumatized Limb		Blood Changes
						Gm	% of Est Bl Vol	
364	16.8	156	17.0	46	2.5	769	45.7	Very slight dilution
373	12.3	120	20.0	70	4.3	609	49.5	Early dilution with slight terminal concentration
375	20.6	126	20.0	76	4.0	1020	49.5	Moderate dilution
380	10.4	126	20.0	44	1.2	505	48.5	Early dilution Terminal concentration
381	12.3	144	22.0	65	2.0	499	40.5	Moderate dilution
Averages		134	19.8	60	2.8	—	46.7	

The amount of fluid lost into the traumatized part, as shown by comparative weights of the hindquarters, averaged 46.7 per cent of the estimated blood volume for the group. This is within the range of the average per cent of the estimated blood volume which is obtained on bleeding to death in comparable time dogs anesthetized with ether, and indicates that the fluid lost was very largely blood. Necropsy revealed considerable bruising and maceration of muscles and subcutaneous tissues and extensive pooling and infiltration of fluid consisting predominantly of blood.

Group 2—In 15 experiments, divided into three series, a 2 per cent solution of procaine was injected intrathetically in amounts sufficient to produce anesthesia in the lower extremities and abdomen and lower the blood pressure to levels within the desired range before the application of trauma. Readings taken from 5 to 15 minutes after injection showed pressures ranging from 82 to 50 Mm Hg, of which 11 were under 76 Mm Hg. These pressures were obtained by a single injection of 3.3 mg/Kg of body weight in seven cases, and by 4.0 mg/Kg in two cases. In the remaining experiments additional injections of varying amounts were necessary to obtain the desired pressure range.

As soon as the pressure had been lowered within the above range the limb was traumatized, and it was noted that the resultant swelling was much less than that produced by a corresponding number of blows in Group 1. Except for four instances, the procedure of Swingle, and associates, of applying more trauma than in the control experiments was followed. The number of blows per Kg of body weight was 25 in each experiment except Nos. 372, 376, 382 and 370, in which instances it was 20. When the blood pressures were read 15 to 20 minutes after trauma they were found in some cases to be lower than before trauma, but in most cases they were appreciably higher.

The readings were taken at a time when the vasodepressor effect of the procaine was usually wearing off. By the end of a 45- to 75-minute period of spinal anesthesia, as indicated by the first return of tail or leg reflexes, the pressure had risen much above the shock level, the traumatized limb showed relatively little further increase in size and the animals were free from evidences of shock. The low blood pressure during and for some time after trauma favored the sealing-off of the opened blood vessels and the early arrest of hemorrhage.

Series 1—In order to determine the amount of local fluid loss from trauma that had been applied at a time of low pressure following a single spinal injection of procaine, five animals were injected, traumatized, and then sacrificed 1.3 to 4.3 hours later. The results are shown in Table II. In

TABLE II

FLUID LOSS IN RIGHT HIND LIMB FROM TRAUMA APPLIED WHILE BLOOD PRESSURE WAS LOWERED BY SINGLE INJECTION OF SPINAL ANESTHETIC. SACRIFICED 1.3 TO 4.3 HOURS AFTER TRAUMA

Dog No	Wgt Kg	Control B P mm Hg	B P After Spinal	B P After Trauma		Sacrificed After Trauma Hrs	Fluid Loss Into Traumatized Limb		Blood Changes
				Hrs	mm Hg		Gm	% of Est Bl Vol	
363	11 1	154	66	0 7	96	4 3	358	32 2	Very slight concentration
372	17 1	144	58	3 5	120	1 7	420	24 6	Early dilution followed by slight concentration
				1 5	116				
376	11 0	154	60	0 3	44	1 3	244	22 2	
				1 3	128				
425	10 0	120	75	0 25	105	1 3	200	20 0	Slight concentration
				1 25	130				
426	12 5	144	82	0 25	72	1 3	268	21 4	
				1 25	134				
Averages		143	68					24 1	

each instance the leg and tail reflexes had returned by the time of sacrifice and the blood pressure had climbed well up toward the control level without resulting in extensive limb swelling. There was little or no evidence of circulatory change beyond a slight to moderate lowering of blood pressure.

The increase in limb volume averaged 24.1 per cent of the estimated blood volume, only slightly more than half that found in the control group, and with but one exception, Dog 363, was below the level at which it might be expected ultimately to produce shock. Necropsy revealed maceration of tissues at the trauma site at least equal to, and in some cases greater than, that observed in the control experiments, but there was a great deal less extravasated blood and plasma. The blood changes were either inconsequential or a slight concentration.

Series 2—To determine the effect of a more continuous spinal anesthesia on the amount of local fluid loss from trauma, five animals were injected intrathecally with procaine, traumatized and then given subsequent injections at intervals varying from 0.75 to 1.25 hours through the needle which had been left *in situ*. The intervals between injections were determined by the first appearance of tail or leg reflexes. Anesthesia was maintained for

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periods of from 3 7 to 4 1 hours The results are shown in Table III The doses after trauma were smaller than the primary dose by two-fifths to three-fifths and usually produced less marked and less prolonged lowering of blood pressure They were sufficient, however, to keep the tail and leg reflexes abolished At the end of the period of anesthesia the relatively high blood pressure and the responsiveness of the animals attested to the absence of shock

TABLE III

FLUID LOSS IN RIGHT HIND LIMB FROM TRAUMA APPLIED WHILE BLOOD PRESSURE WAS LOWFRED BY SPINAL ANESTHESIA ANESTHESIA PROLONGED 3 7 TO 4 1 HOURS BY REPEATED INJECTIONS SACRIFICE 4 TO 5 8 HOURS AFTER TRAUMA

Dog No	Wgt Kg	B P mm Hg			Duration of Spinal Anesthesia	B P After Trauma		Sacrificed After Trauma Hrs	Fluid Loss Into Traumatized Limb			Blood Changes
		Control	10-15 Min After Spinal Anesthesia	3 Hrs After Trauma		Hrs	mm Hg		Gm	% of Est Bl Vol		
382	11 1	130	80	3 7	0 4 4 0 5 7	70 107 96	5 8	248	22 3		No change first 2 hrs Concentration to 4th hr , then moderate dilution	
427	13 6	125	74	4 1	0 2 4 0	80 112	4 3	507	37 3	}	Slight dilution then concentration	
428	15 3	144	78	4 0	0 2 4 0	104 138	4 0	335	21 9			
431	13 2	116	66	4 0	0 2 4 0	100 118	4 2	231	17 5			
434	12 1	110	64	4 0	0 3 4 3	50 116	4 3	166	13 7		Moderate dilution	
Averages		125	72	4 0			4 5		22 5			

Sacrifice was made 4 0 to 5 8 hours after trauma and the increase in limb volume averaged 22 5 per cent of the estimated blood volume This is further evidence of the early arrest and smallness of the hemorrhage resulting from the trauma under condition of low blood pressure Necropsy revealed that the maceration of tissues and extravasation of blood and plasma were similar in amount to the findings in Series 1 of this group The red blood count, hemoglobin and hematocrit changes were not marked in any case

Series 3—In order to determine the ultimate effects on the circulation of limb trauma performed under a more continuous spinal anesthesia, five dogs were treated as were those in Series 2 except that, instead of being sacrificed at the end of the three- to four-hour period of spinal anesthesia, they were given the opportunity to survive After taking blood pressures and blood samples, they were returned to their cages five to seven hours from the time they were restrained on the table, and then given food and drink The limb swelling appeared to be about equal to that seen in Series 2, and all animals were free from shock The results are shown in Table IV

On the following morning they had recovered from the general effects of the experiment, and their blood pressures registered in the vicinity of normal The traumatized limb was much more swollen than on the previous afternoon After taking blood samples and pressures, the animals were sacrificed and necropsied There was little or no gross evidence of visceral

changes Incisions of the traumatized limbs revealed the presence of blood and macerated tissue, and in addition, a considerable amount of edematous fluid This late shift of fluid to the traumatized part took place concomitantly with the drinking of water and did not impair the general circulation

TABLE IV

DOGS SURVIVING RIGHT HIND LIMB TRAUMA APPLIED WHILE BLOOD PRESSURE WAS LOWERED BY SPINAL ANESTHESIA ANESTHESIA PROLONGED 3 TO 4 5 HOURS BY REPEATED INJECTIONS SACRIFICE FOLLOWING DAY

Dog No	Wgt Kg	Duration of Spinal Anesthesia After Trauma Hrs	Blood Pressure—mm Hg					Remarks
			Control	10-15 Min After Spinal Injection	15 Min After Trauma	3 7 to 4 8 Hrs After Trauma	22 5 to 24 0 Hrs After Trauma	
370	18 3	3 5	144	76	80	124	124	No shock Recovered Drank 1200 cc water Sacrificed 23 hrs
409	11 5	3 0	150	54	56	100	116	No shock Recovered Drank 1600 cc water Sacrificed 22 5 hrs
421	9 7	4 5	158	50	70	98	140	No shock Recovered Drank 900 cc water Sacrificed 22 3 hrs
423	8 1	4 0	135	75	100	126	154	No shock Recovered Drank 1800 cc water Sacrificed 24 hrs
424	11 1	3 0	120	71	108	116	120	No shock Recovered Drank 800 cc water Sacrificed 23 3 hrs
Averages		3 6	141	65	83	113	131	

The blood changes are shown in Table V The only consistent change was a moderate dilution between the last determinations in the afternoon and those of the following morning, which came about with the taking of fluids During the first four hours of the experiment the changes were either inconsequential or slight to moderate concentration

Group 3—In 18 experiments the blood pressures of the limb to be traumatized were reduced, with two exceptions, to a level of 73 Mm Hg, or

TABLE V

BLOOD STUDIES ON DOGS SHOWN IN TABLE IV

Exp No	Control Sample	Samples after Trauma Hrs			
		0 3	1 8 to 2 8	3 3 to 4 8	22 to 24
370	R B C M	7 24	6 40	7 60	7 94
	Hb Gm	16 5	14 6	16 8	15 4
	Hcr %	49 5	43 0	49 0	50 5
409	R B C M	7 32	7 50	8 60	8 28
	Hb Gm	15 0	15 3	17 4	16 9
	Hcr %	45 5	46 5	51 5	50 0
421	R B C M	6 56	6 46	6 40	6 72
	Hb Gm	14 7	14 5	14 2	14 9
	Hcr %	43 0	43 0	42 5	44 0
423	R B C M	7 00	7 48	7 64	7 26
	Hb Gm	15 0	15 5	16 0	15 0
	Hcr %	43 5	47 0	48 0	46 0
424	R B C M	6 23	6 51	6 46	6 64
	Hb Gm	12 6	13 0	12 9	13 2
	Hcr %	37 0	39 0	39 0	39 5

below, by ligation of the iliac artery and one or more proximal branches of the femoral artery through an incision just above and parallel to Poupart's ligament. The iliac was first ligated and the blood pressure in the femoral artery then obtained. If the pressure was not below 76 Mm Hg, the profunda femoris was then tied. This usually sufficed, but in a few cases ligation of other proximal branches was required in order to attain lower levels. In some cases the reduction of pressure was below the levels produced by spinal anesthesia in Group 2, but the average for the group was 63 Mm Hg. The experiments were divided into three series for comparison with those in Group 2.

Series 1—Studies were made in eight dogs of the early effects on the circulation and limb volume of trauma applied following arterial ligation, but with the nerves left intact. The results are shown in Table VI.

TABLE VI

FLUID LOSS IN RIGHT HIND LIMB FROM TRAUMA APPLIED WHILE ITS BLOOD PRESSURE WAS LOWERED BY PERMANENT LIGATION OF THE ILIAC ARTERY AND ONE OR MORE PROXIMAL BRANCHES OF THE FEMORAL ARTERY
SACRIFICE 1 1 TO 2 2 HOURS AFTER TRAUMA

Femoral Artery Blood Pressure mm/Hg									
Exp No	Wgt Kg	Amount of Trauma Blows/Kg	Left		Right After Ligation		Sacrificed After Trauma Hrs	Fluid Loss Into Traumatized Limb	
			Before Trauma	1 Hr After Trauma	Before Trauma	1 Hr After Trauma		Gm	% of Est Bl Vol
387	10 1	20 0	150	106	54		1 1	272	26 9
390	8 3	20 0	140	116	70	34	2 2	81	9 8
				(2 hrs 110)					
391	10 2	25 0	170	120	70	38	1 2	172	16 9
393	10 4	25 0	150	130	52	32	1 2	60	5 8
397	9 7	25 0	130	100	54	30	1 4	28	2 9
398	10 2	25 0	150	120	52	32	1 4	96	9 4
399	21 2	25 0	170	135	120	64	1 4	700	33 0
404	9 3	25 0	145	110	28	28	1 5	72	7 7
Averages			150	116	63	37			

The trauma consisted of 25 blows per Kg body weight except in experiments Nos 387 and 390, where it was 20 blows per Kg. Blood pressures were taken from the right and left femoral arteries both before and one hour after trauma (two hours in one case) and blood samples were obtained from the left femoral artery at the same time. It was noted that limb swelling was very slight in most cases, and while there was a moderate reduction in blood pressure one hour after trauma, there were no indications of shock.

The animals were sacrificed 1 1 to 2 2 hours after trauma. Comparison of weights of the hindquarters revealed much variation, but, on the whole, considerably less increase in volume of the traumatized side than was found in Series 1 of Group 2. This was due to the more complete interference with the limb circulation by the permanent ligations, and also to injury of collateral vessels by the trauma, as indicated by the very low pressure readings in the right femoral artery one hour after trauma. Incisions of the traumatized region showed much bruising of tissues but usually relatively little extravasa-

tion of blood or plasma The red count, hemoglobin and hematocrit determinations revealed very little blood change

Series 2—In five dogs subjected to ligation followed by limb trauma of 25 blows per Kg of body weight, the procedures and findings were the same as in the above series during the first hour following trauma At this point, however, the ligatures were removed in order to simulate the conditions in Series 1, Group 2, where the blood pressure rose with the wearing-off of the single spinal anesthetic The results are shown in Table VII

TABLE VII

FLUID LOSS IN RIGHT HIND LIMB FROM TRAUMA APPLIED WHILE ITS BLOOD PRESSURE WAS TEMPORARILY LOWERED BY LIGATION OF THE ILIAC ARTERY AND ONE OR MORE PROXIMAL BRANCHES OF THE FEMORAL ARTERY
LIGATURES REMOVED ONE HOUR AFTER TRAUMA SACRIFICE 2 5 TO 3 1 HOURS AFTER TRAUMA

B P Right Femoral A
mm Hg

Exp No	Wgt Kg	B P Left Femoral A mm Hg			While Ligated		After Ligature Removed		Sacrificed After Trauma Hrs	Fluid Loss Into Traumatized Limb		
		Before Trauma	1 Hr After Trauma		Before Trauma	1 Hr After Trauma		10 Min After Removal	Just Before Sacrifice		%	
			Before	After		Before	After				Gm	Bl Vol
394	19 0	146	130	104	72	50	122	106	2 5	420	22 0	
395	22 2	135	110	110	73	40	110	110	2 5	560	25 2	
400	15 5	150	140	125	70	48	140	120	2 5	451	29 1	
405	17 7	145	130	130	72	48	130	125	3 1	270	15 5	
408	18 1	160	130	110	84	46	120	110	3 0	380	21 0	
Averages		147	128	116	74	46	124	114	2 7		22 6	

Upon removal of the ligatures the pressure in the femoral artery rose promptly to the general level of that obtained in the opposite limb one hour after trauma, and the limb subsequently showed only slight evidence of further swelling Just previous to sacrifice, 2 5 to 3 1 hours after trauma, the animals were found to have moderate reductions in blood pressure, similar to those of Series 1, Group 2, and, likewise, there were no signs of shock Comparison of weights of the hindquarters revealed approximately the same amount of fluid loss into the traumatized limb as was found in Series 1 and 2 of Group 2 Expressed in terms of the estimated blood volume, it was less than one-half of the percentage lost in control Group 1 Incisions of the traumatized region revealed extensive maceration of tissues and only a moderate amount of extravasated blood Blood studies showed either no change or a very slight concentration

Series 3—Five experiments were performed in order to elicit the long-term effects of trauma to the right hind limb with its blood pressure lowered by arterial ligation and its nerve pathways intact The results are shown in Table VIII The arteries were exposed and tied and the wound closed, using aseptic technic, after which 25 blows per Kg of body weight were applied Back pressure in the right femoral artery was read only immediately after ligation The animals were kept restrained on their backs on the table for four to five hours and during this time the blood pressure, as measured in the left femoral artery, remained either up to the control level or was only moderately reduced The traumatized limb became slightly to moderately

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swollen When the dogs were returned to their cages they moved about with little difficulty and drank water freely The following morning they had recovered from the general effects of the experiment and the blood pressures were found to be very slightly to moderately reduced from the initial pressures Sensation was intact in the traumatized limbs and considerably more

TABLE VIII

DOGS SURVIVING RIGHT HIND LIMB TRAUMA APPLIED WHILE BLOOD PRESSURE OF TRAUMATIZED LIMB WAS LOWERED BY PERMANENT LIGATION OF THE ILIAC ARTERY AND ONE OR MORE BRANCHES OF THE FEMORAL ARTERY SACRIFICE FOLLOWING DAY

Femoral Artery B P mm Hg							
Exp No	Wgt Kg	Left Initial	Right After Ligation	Left Hrs After Trauma			Remarks
				1	4-5	21-24	
396	17 5	155	46	130	130	150	No shock Recovered Drank 2,100 cc water Sacrificed 22 5 hrs
407	10 6	160	58	130	130	125	No shock Recovered Drank 1,700 cc water Sacrificed 22 0 hrs
410	17 2	128	58	128	124	115	No shock Recovered Drank 600 cc water Sacrificed 21 8 hrs
413	17 3	180	44	130	180	148	No shock Recovered Drank 1 400 cc water Sacrificed 22 5 hrs
414	12 5	166	38	110	136	135	No shock Recovered Drank 1,400 cc water Sacrificed 23 5 hrs
Average		158	49	126	140	135	

swelling had occurred, as was found in Series 3 of Group 2 Incisions after sacrifice revealed macerated tissues, blood and edema in the traumatized regions and considerable swelling of nontraumatized tissues above and below the site of trauma The blood changes in the early period were variable and relatively slight, but a slight to moderate dilution was present in all cases on the following morning, as shown in Table IX

DISCUSSION—The results in Group 1 are in line with the generally recognized findings in limb trauma experiments that produce death within a few hours The local fluid loss of an average of 46 7 per cent of the estimated blood volume is within the range of the average blood loss when anesthetized dogs are bled to death in comparable periods of time The rapid swelling of the limb during and shortly after the trauma, the low blood pressure read ten minutes after trauma, and the necropsy findings of large amounts of extravasated blood constitute convincing evidence that the predominant cause of the shock and death was the loss of blood into the limb Because of the more marked and sustained vasodepression and the earlier death, it is apparent that the trauma was somewhat more severe than in the experiments of Swingle, and associates

The results in Group 2 confirm the observation of Swingle, and coworkers, that limb trauma even greater than that required to produce fatal shock in dogs anesthetized with ether during the traumatization does not produce shock or

death if the trauma is applied while the animals are under ether and the blood pressure has been lowered to 75 Mm Hg, or less, by spinal anesthesia. But a different explanation was found for these results.

TABLE IX
BLOOD STUDIES ON DOGS SHOWN IN TABLE VII

Exp No	Control Sample		Samples After Trauma Hrs			
			0 5	1 0	5 0	22 to 24
396	R B C M	9 30	8 60	8 76	8 44	7 60
	Hb Gm	18 5	17 1	17 2	16 9	15 6
	Hcr %	52 5	50 0	50 0	51 0	46 0
407	R B C M	9 52	9 90	10 16	9 70	8 94
	Hb Gm	19 5	20 3	20 7	19 8	18 3
	Hcr %	57 5	60 5	61 0	59 0	53 0
410	R B C M	7 80	8 10	8 44	8 04	7 50
	Hb Gm	15 9	16 5	17 3	16 5	15 3
	Hcr %	47 5	49 0	49 5	49 5	45 5
413	R B C M	5 56	5 36	5 26	5 40	4 42
	Hb Gm	11 4	11 0	10 8	11 1	9 3
	Hcr %	32 0	31 5	31 0	32 0	26 5
414	R B C M	7 94	7 30	7 44	6 64	5 70
	Hb Gm	15 1	13 9	14 1	13 0	11 7
	Hcr %	44 0	41 0	41 5	38 0	38 0

Comparison of the weights of the two hindquarters of animals sacrificed soon after either the single or the more continuous spinal anesthesia revealed that the amount of fluid lost into the traumatized limb was approximately but one-half as great as that in Control Group 1. The loss of that amount of fluid (which necropsy showed to be very largely blood) was enough to account for the slight to moderate vasodepression present at the time of sacrifice, but it was not enough to produce shock. The protection against hemorrhage afforded by the low blood pressure from blockage of vasomotor and motor nerves is sufficient explanation for the failure of development of shock and the survival of Series 3. The assumption of important additional protection from the blockage of nociceptive stimuli from the regions of trauma is not warranted.

Just how nociceptive stimuli act in creating shock has not been clearly set forth by the proponents of the theory. From the limb they would pass by the sensory pathways to the cerebrum, principally the cortex, and if it is presumed that further action is through the sympathetics, efferent impulses would then go to the medullary and hypothalamic vasomotor centers and lower the blood pressure. But if spinal anesthesia blocks a flow of nociceptive stimuli from the traumatized limb to the brain and thereby prevents a fall in blood pressure and shock from occurring, it also simultaneously produces a fall in blood pressure by blocking the vasomotor and, very much less importantly, the motor fibers of the spinal roots, which would unquestionably tend to offset the benefits of the first-mentioned action.

When the blood pressure is low from spinal anesthesia and large arteries are opened by the injury to the limb, there may be enough blood loss to constitute the predominant cause of shock and death. This was the case in the three experiments excluded from the three groups. Twenty-five blows

per Kg of body weight were delivered. In one the femoral artery was torn early in the course of the trauma and a large hematoma collected subcutaneously on the front of the thigh. Death resulted in 2.9 hours and the increase in limb volume equalled 41.2 per cent of the estimated blood volume. In two cases the femur was broken. Death occurred in one of these in 3.9 hours, and the increase in limb volume equalled 30.0 per cent of the estimated blood volume. The other one died after being returned to the cage for the night and the increase in limb volume equalled 35.0 per cent of the estimated blood volume.

The results in Group 3 further challenge the correctness of the view that nociceptive nerve stimuli are an important cause of experimental limb trauma shock. With the nerves intact in this group, the flow of nociceptive stimuli from the traumatized field should have been at least as great as in Group 1, and greater than in Group 2, because of the periods of spinal anesthesia. And still none of the animals developed marked lowering of blood pressure or other manifestations of shock. The objection might be raised that the nerves of the traumatized limb in Group 3 would be less sensitive to stimuli during and shortly after the trauma than those in Group 1 because of the greater average lowering of blood pressure and interference with nutrition. However, as the early pressure levels of the traumatized limbs of the dogs of these two groups were comparable in some cases, and the trauma was greater by 25 per cent in 16 of the 18 experiments in Group 3, this should have compensated for any reduced sensitivity. In all three series the general blood pressure one hour after traumatization was slightly to moderately reduced except in one experiment. In Series 2 the reduction was either maintained or slightly augmented 2.5 to 3.1 hours later, but in Series 3 there was a tendency to elevation of pressure in four to five hours. The changes in pressure may well have been due to the local fluid loss except in four of the cases of Series 1, where it was too small to have been the sole factor.

From a survey of the findings it is apparent that when the limb of an animal is traumatized at a time when its blood pressure is greatly lowered, there is a definite protection against shock because of local hemorrhage being considerably less than is the case when the blood pressure is at a normal level. The results were about the same whether the nerve impulses from the limb were blocked, as when spinal anesthesia was used, or not blocked, as when the arteries were ligated, so long as the blood pressure in the limb was kept at comparably low levels.

When these findings are considered along with previous findings that direct stimulation of the large nerves of the limb may be kept up for hours without causing a significant fall in blood pressure, and that stimulation of the carotid sinus and aortic depressor nerves may maintain a low blood pressure for as much as several hours without serious impairment of the circulation,¹⁰ the evidence is strong that afferent nerve impulses from the field of injury are not factors of great importance in limb trauma shock of the type described here.

The experiments deserve consideration from the standpoint of a toxic factor in traumatic shock. If toxins are formed in the traumatized tissues, the greater the degree of trauma the greater should be the amounts produced. If this is true, the animals in Group 1, which received an average of 20 blows per Kg of body weight, should have shown no more toxic effects than did the great majority of those in Groups 2 and 3, which received 25 blows per Kg of body weight. Since the local loss of fluid was so evidently the predominant cause of circulatory embarrassment and death in Group 1, and since any circulatory damage that may have occurred in the more severely traumatized Groups 2 and 3 was so minimal as not to cause shock or death, there is little reason to believe that, if toxins were formed in the damaged tissues, they were an important cause of the circulatory difficulties of animals in any of the three groups.

EFFECTS OF CORD, NERVE AND DORSAL ROOT SECTIONS

If, as was reported by Swingle, and coworkers, the complete and permanent blockage of all impulses from the traumatized regions by preliminary section of the nerves of limbs or of the spinal cord at T-13/L-1 does not prevent limb trauma shock of the type described, while temporary blockage for four hours by local procaine injections and for two hours by tourniquet constriction prevents shock, the reason could not possibly be blockage of nociceptive stimuli. They postulated that the nerve or cord sections had permanently removed some nervous factor tending to maintain the resistance of the animal to shock. In consequence they made studies of a variety of partial sections of the spinal cord at T-13/L-1 in an attempt to obtain more specific information regarding the site of a factor, the lack of which apparently sensitized the traumatized dog to shock.

Section of either the anterior or posterior half of the cord failed to prevent the occurrence of shock, but if the ventrolateral areas of the anterior half were cut while the ventromesial areas were preserved, the animals were protected from shock. The ventrolateral areas appeared to be the most important areas in the production of shock. The ventrolateral areas include, among others, the dorsal spinothalamic ascending tracts which transmit pain stimuli and are also presumed to transmit nociceptive stimuli. It was reported that the descending tracts contained in the ventromesial areas of the cord are concerned in maintaining the resistance of the animal to shock from muscle trauma. Destruction of these areas might result in vasodilatation of the blood vessels distal to the cut, produced either directly or indirectly through loss of muscle tone. This vasodilatation should increase the fluid loss into the limbs during the actual traumatization by an amount sufficient to be an important factor in the production of shock.

If impulses passing over the descending tracts in the ventromesial areas of the cord protect against shock from limb trauma, and if nociceptive stimuli passing over the pain or other afferent fibers of the dorsal spinothalamic or other tracts interfere with this protection, as suggested by the authors,

then preliminary section of the dorsal spinal roots, thereby interrupting all afferent impulses from a limb, should protect against shock from trauma applied to that limb

This premise was tested experimentally on four dogs as follows. Under intravenous evipal anesthesia a laminectomy from T-13 to S-1 was performed, the dura opened and all dorsal roots on the left side below T-12 were sectioned. Aseptic technic was used except on one animal which was experimented on acutely. Because of considerable degrees of hemorrhage in experiments Nos. 333, 341 and 345, electrocoulometric determinations were made

TABLE X
SHOCK FROM TRAUMATIZING LIMB AFTER SECTION OF ITS DORSAL SPINAL NERVE ROOTS

Exp No	Wgt Kg	Initial Pressure mm Hg	Elapsed Time Between Root Section and Trauma	Blood Pressure Before Trauma mm Hg	Amount of Trauma Blows/Kg	Survival Period Hrs	Fluid Loss Into Traumatized Limb		Blood Changes
							Gm	% of Est Bl Vol	
333	13.3	116	4 hours	98	15.0	1.8	464	34.9	
341	7.9	150	2 days	116	17.1	1.5	372	47.3	Moderate dilution
338	9.4	140	3 days	156	18.6	1.9	446	47.4	
345	11.3	164	6 days	130	11.0	3.3	520	46.0	Slight dilution

of the amounts of blood lost on the sponges and drapes and equivalent transfusions were given. Left limb trauma under ether was applied four hours and two, three, and six days after dorsal root section. All animals were in relatively good general condition at the start of the trauma. The trauma was made somewhat more severe by the use of heavier blows than was given in the three groups reported above, as it was the intention to produce rapid circulatory embarrassment and early onset of shock. The results are shown in Table X.

The average period of survival was somewhat shorter than in Group I, but the average amount of local fluid loss into the limb in terms of per cent of the estimated blood volume was approximately the same in both groups except for the acute experiment, No. 333, where only four hours had elapsed between the surgery and trauma. Red blood count, hemoglobin and hematocrit determinations revealed very slight to moderate blood dilution.

Contact with the cord during surgery was avoided as much as possible in order to prevent injury and in no case was there instrumentation of the ventromesial areas. Consequently, the descending tracts in the ventromesial areas of the cord were left intact while the fibers of the dorsal spinothalamic and all other tracts which might transmit pain and presumable nociceptive stimuli were destroyed.

There appeared to be no concrete evidence in these experiments that the animals were protected against shock by destruction of the pain and other afferent fibers of the cord by dorsal root section, even though the descending tracts of the ventromesial areas were left intact, since they tolerated trauma and blood and plasma loss into the limb no better than did the normal dogs of Group I.

SUMMARY

Experiments were conducted on dogs in an endeavor to determine the relative rôles of nerve impulses and local fluid loss in the production of shock due to limb trauma. They were undertaken because of work reported by Swingle, and associates, which indicated that a flow of nociceptive stimuli from the traumatized regions, unless prevented by spinal anesthesia or a local block, is an important contributing factor in the initiation of the shock state which follows. The spinal anesthetic lowered the blood pressure to 75 Mm Hg, or under, before the trauma was applied.

The experiments were divided into three groups, the trauma was limited to one limb and the local fluid loss was determined by comparison of the weights of the hindquarters. Trauma was applied during ether anesthesia and consisted of moderate blows from a padded hammer.

In Group 1 it was applied with the nerve pathways intact and the systemic blood pressure at normal levels. An average of 20 blows per Kg of body weight caused rapid and marked swelling with early onset of shock and death after an average of 28 hours. The fluid loss into the limb, consisting predominantly of blood averaged 46.7 per cent of the estimated blood volume. It was obviously the outstanding cause of shock and death.

In Group 2 the trauma was applied after the nerve pathways to the hind limbs and lower trunk were blocked by spinal anesthesia and the blood pressure lowered to 75 Mm Hg, or under. In the majority of experiments 25 blows per Kg of body weight were used, but in a few it was limited to 20, as in Group 1. The swelling was much less marked than in Group 1, and in no instance did shock develop. In those animals sacrificed shortly after periods of either single injection or continuous spinal anesthesia the local fluid loss was approximately one-half that found in Group 1, and it was not sufficiently large to produce shock. The animals which were allowed to survive were in good general condition on the following day.

In Group 3 the trauma was applied with the nerve pathways to the limb intact and with the blood pressure in the limb lowered to an average of 63 Mm Hg by arterial ligations. The number of blows, with two exceptions, was 25 per Kg of body weight. The amount of swelling was either comparable with or less than that found in Group 2, and in those experiments in which the ligatures were removed one hour after trauma, there was little additional swelling apparent. This was indicative of early arrest of hemorrhage occurring while the limb pressure was low. The systemic blood pressures were in some instances slightly to moderately reduced, but in no case did shock develop. In those animals sacrificed 11 to 31 hours after trauma the local fluid loss, with a few exceptions, was less than half that of control Group 1, and was not enough to produce shock. The animals that were allowed to survive were in good condition the following day.

In Group 1 the rapid swelling of the limb and the large amount of local fluid loss (which at necropsy was found to be blood in very large measure) are

evidence that factors other than hemorrhage did not play an important part in the production of shock and death

In Group 2 the animals were protected from shock through the action of the spinal anesthetic in blocking the vasomotor and (less importantly) motor nerves, lowering the blood pressure and reducing the hemorrhage below a level that produces shock. There was no evidence that blockage of nociceptive stimuli was an important factor in preventing shock.

In Group 3 the trauma was greater than in Group 1, and as the nerves were intact, the flow of nociceptive stimuli should, therefore, have been as great as or greater than in Group 1. Still shock did not develop.

There is no evidence in these experiments of an important action from toxins formed in the damaged tissues since, if present, it should have been manifest in Groups 2 and 3, where the trauma was greater than in Group 1, while in Group 1 the onset of shock was too rapid to have been caused by it.

Swingle, and coworkers, confirmed the work of others that section of the nerves to the limbs or of the spinal cord at T-13/L-1 does not prevent shock from limb trauma. This would preclude the possibility that any protection obtained from procaine injections of the nerves or tissues was the result of blockage of nociceptive stimuli from the traumatized regions.

The theory that the descending tracts of the ventromesial areas of the cord protect against limb trauma shock but that afferent nociceptive stimuli from the legs, apparently transmitted by the ventrolateral cord regions, eliminate this factor and sensitize to shock, was tested experimentally as follows. The left dorsal spinal nerve roots below T-12 were sectioned, which destroyed all afferent impulses from the left limb. When the limb was subsequently traumatized there was no sign of protection against shock, as the animals tolerated blood loss and tissue damage no better than did the normal dogs of Group 1.

CONCLUSIONS

1. No evidence was obtained from these limb trauma experiments that either a flow of nociceptive stimuli from the injured field or toxin formation is an important contributing factor in the initiation of any circulatory impairment or shock which followed.

2. The animals in which the trauma was applied soon after the administration of a spinal anesthetic were protected from shock principally by the blockage of the vasomotor and (less importantly) motor nerves, which greatly lowered the blood pressure and limited the hemorrhage to an amount that was too small to produce shock, instead of by the blockage of afferent impulses. The maintenance of such a low blood pressure by spinal anesthesia for the prevention of shock during an operation on man is contraindicated as the amount of anesthetic required would be too toxic.

3. In all of the experiments where shock developed the local blood loss was large and constituted the outstanding causative factor.

4. There appears to be no indication for the renewal of efforts to prevent shock by the blockage of afferent nerve impulses through the use of local

or spinal anesthesia Indications for the use of local or spinal anesthesia in shock are based on other grounds

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STAINLESS STEEL WIRE-MESH IN THE REPAIR OF SMALL CRANIAL DEFECTS¹

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SMALL CRANIAL DEFECTS, those ranging in size from bur holes to openings of approximately two inches in diameter, have excited little attention in the past but rather have been shrugged off as of no serious consequence. Yet bur holes in the frontal region uniformly result in unsightly depressions

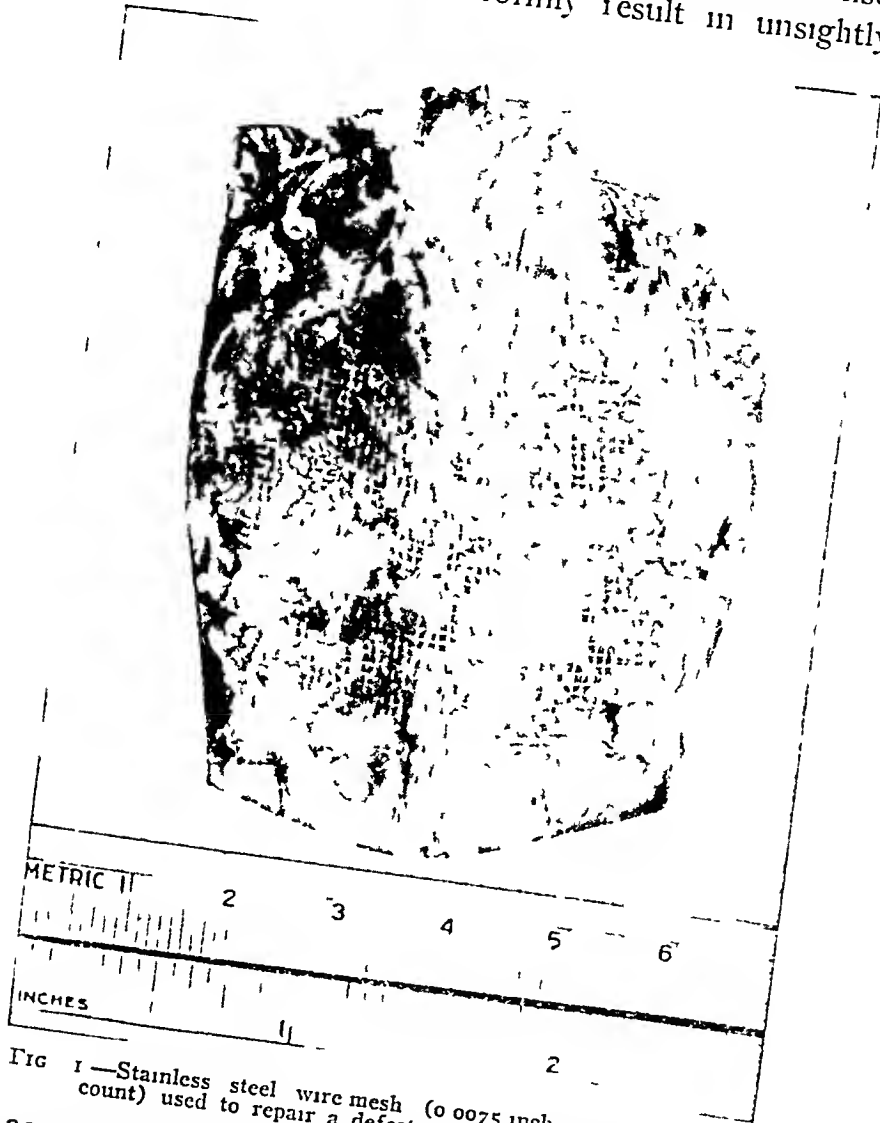


FIG 1—Stainless steel wire mesh (0.0075 inch wire, 28 × 28 count) used to repair a defect in the skull of a dog

and may be associated with tenderness, especially when filaments of the supra-orbital nerve pass over them. Defects larger than bur holes, but generally less than two inches in diameter, are usually the result of trauma or of small craniectomies, such as are performed for tumors of the skull or drainage of an abscess of the brain. Unless these defects are in the

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forehead they generally constitute no cosmetic problem. At any site, however, they may be tender or spontaneously painful, the pulsation frequently is an annoyance to the patient and the justified fear of injury to "the soft spot" in the head is a constant source of worry.

Bur holes in the frontal region have been filled with bone dust or by buttons removed with the trephine, but these bits of bone absorb rapidly and so fail in the purpose for which they are used. Some, including this

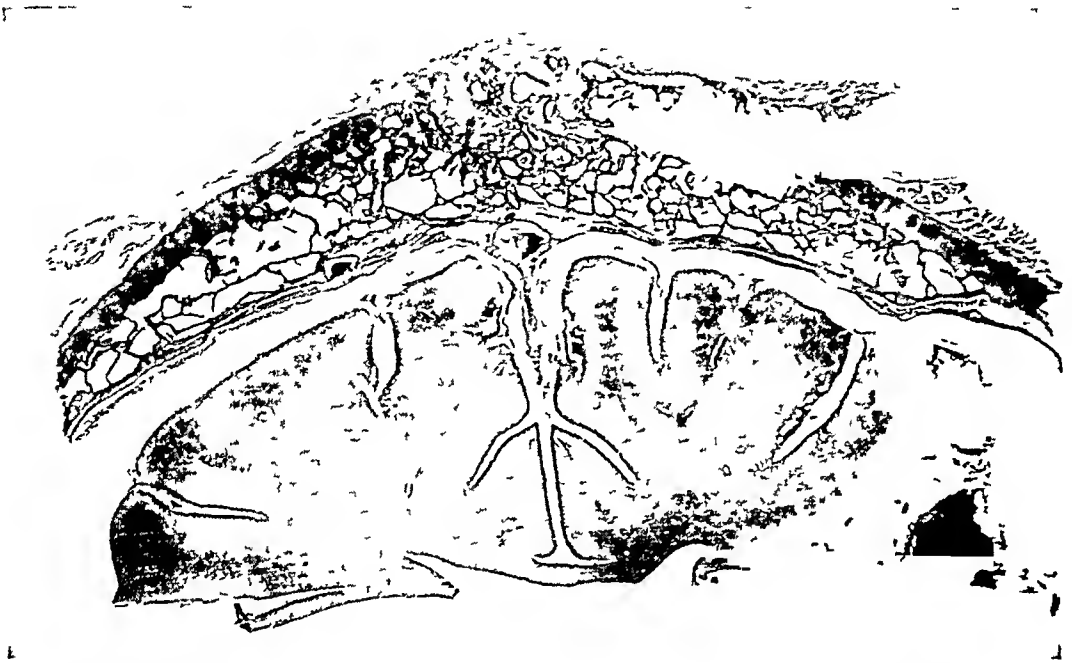


FIG. 2.—Cross section through the repaired defect in the skull. The mesh was laid on the outer surface of the dura and of the skull. No evidence of irritation of the meninges or brain could be seen. The demonstrable proliferation of bone between the two layers of screen is regarded as being peculiar to the dog.

writer, have regarded the use of bone fragments and dust as actively contraindicated because of the frequency of associated infection.

Slightly larger defects have excited still less attention. In those which follow trauma it has been the custom to replace larger bone chips which, because of their size, are more likely to develop an adequate blood supply, unite with the skull, and prove satisfactory. Other openings of small size have seldom seemed to justify the use of vitallium, tantalum or lucite, which have seen such increasing use in the larger and more surgically attractive group of deficiencies in the skull. Virtually, the small openings have been ignored as necessary evils.

Stainless steel wire has long been recognized as an inert substance in tissues. In the skull it does not show the disadvantages attributed to it when it is used for orthopedic purposes in other bones of the body. Wire used to hold osteoplastic bone flaps in position or in myoplastic craniotomies becomes tightly embedded within the bone as osseous repair takes place. It seemed reasonable that a mesh of stainless steel wire could become anchored in connective tissue and possibly in bone at the edges of a cranial defect.

REPAIR OF CRANIAL DEFECTS

Likewise, the projection of strands of connective tissue into the meshes of the screen, further strengthening and stabilizing the repair, seemed probable. Accordingly, in March, 1942, the Pilling Company made up, on request, strips of stainless steel wire screen with 0.0065-inch wire (40 x 40 and 70 x 70 count) and 0.0075-inch wire (60 x 60 and 28 x 28 count)



FIG 3 —Epidural and epicranial layers of screen covering a bur hole in the exposed frontal region

The mesh was tried first in large dogs. A midline craniectomy was performed, extending from the frontal sinus to a point proximal to the occipital protuberance and about 2.5 cm on either side of the midline. A layer of screen was then placed against the dura, being held in place against the bone by the force of intracranial pressure. A second layer was placed outside of the skull and fastened with sutures to the adjacent periosteum. The postoperative course of all dogs was satisfactory. After periods of from five to eight months the animals were sacrificed. The edges of all strips were firmly bound to bone by connective tissue. Connective tissue had not penetrated the meshes of the two high-count screens, however, and these did not seem to be so firm as were the repairs utilizing the lower-count screens. The latter had been freely penetrated by connective tissue (Fig 1) and, when tapped with an instrument, sounded almost as firm as if they were part of the skull. Subsequently, this was proved to be caused in large



FIG 5—Repair by single epidural mesh of defect resulting from removal of a tumor of the skull



FIG 4—Single epidural layer of mesh repairing a posttraumatic defect in a child, age 2
Clinical demonstration of the defect was not possible one year after repair

part by the spread of bony tissue between the two layers of metal. Cross-section through brain, meninges, calvarium and screen showed but slight dural thickening, no adhesions, no change in the sagittal sinus and no evidence of any harmful effect upon the brain (Fig 2)

Accordingly, the use of both the 0.0065-inch (40 x 40) and 0.0075-inch (28 x 28) screen was begun in patients. During the past 18 months it has been used for small defects as outlined and has been regarded as satisfactory. No ill effects referable to it have been seen or reported. None of these patients has died, or has required further surgery in the same region, so that no human pathologic material is available. In general, the finer wire and mesh have seemed easier to work with, and more promising in result than has the coarser type.

The size of the piece is determined by direct measurement at the operating table. It is cut from a large strip with heavy curved surgical scissors kept for this purpose. The mesh should be held away from the field while being tailored so that bits of wire will not fall into the wound to act as a potential source of irritation. When used to cover frontal bur holes, a layer of screen is placed between the dura and skull before the bone flap is replaced. This remains in position without sutures. Another piece is added outside the skull (Fig 3), as the double mesh seems to give a better cosmetic result.

In the repair of the larger openings resulting from trauma (Fig 4), drainage of an abscess or the removal of a tumor of the skull (Fig 5), the screen has been slipped through notches in the edge of the bony defect into a position between the dura and the skull, or has been placed over the outside of the opening where it is anchored by sutures of cotton, silk or wire to the adjoining pericranium. Care must be maintained that the edges of the mesh outside of the skull do not stick up to irritate the scalp. A single layer of the wire screen has resulted in a firm, painless support for the scalp, which compares favorably with that offered by adjacent bone. When the cosmetic result is a factor, however, a layer of mesh inside and outside of the skull is more likely to preserve a satisfactory contour.

Within its limitations, therefore, this mesh appears to offer a safe, adaptable and readily available method of dealing with small cranial defects.

FRACTURE OF THE ATLAS

REVIEW AND PRESENTATION OF DATA ON EIGHT CASES

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FRACTURES OF THE ATLAS are notable as regards their apparent rarity of occurrence and their comparatively favorable prognosis Hatchette¹ noted 99 cases reported to 1941, and added one of his own Crooks and Birkett² have since reported four cases Eight cases have been encountered at the Mayo Clinic, bringing the total to 112 In 50 of these the lesion has been an isolated fracture of the atlas and in 62 it has been complicated by other injuries, such as fractures of the vertebrae or the skull It is reasonable to suspect that these fractures are more numerous than these figures indicate but are overlooked because of the erroneous impression that the outcome of the fracture of the atlas is quickly fatal, the mortality rate of 10.7 per cent in the cases reviewed to date establishes this entity as dangerous but by no means necessarily fatal

Jefferson³ noted that these fractures are almost always due to trauma to the top of the head when the spinal column is fixed in a neutral position If the spinal column is flexed or hyperextended the injury occurs in areas of mobility, usually the lower cervical or the thoracolumbar region Causes of such injuries have usually been falls or blows on the head⁴, accidents in fast-moving vehicles may also produce this picture, as has been pointed out by Plaut⁵ In a few of the cases summarized by Jefferson⁶ the fracture was due to direct trauma on the back of the neck The infrequency of this mechanism may be explained by the excellent protection given the atlas by the overlying skull and mandible, by the protruding spinous process of the axis and by the thickness of the soft tissue of the back of the neck In one case reported by Crooks and Birkett² and in one of our cases, fracture was due to sudden twisting of the neck while swimming under water

A general knowledge of the anatomy of the atlas is essential for an understanding of the nature of the fracture and its prognosis The atlas is merely a ring of bone, its centrum having migrated to form the odontoid process of the axis Its superior and inferior articular facets face obliquely so that the lateral masses are wedge-shaped with their bases lateral Thus, any compression force on the bone tends to cause it to spread outward, this being resisted by the anterior and posterior arches and the transverse ligament If the force is too great the ring breaks, usually in the posterior arch as (1) this is weakened by the grooves for the vertebral arteries, and (2) the posterior and lateral facing of the occipital condyles tends to splay the

atlas out in those directions (Fig 1a) Thus the fracture produces a widening of the arch resulting in a decompression of the spinal cord in this area

Clinical signs are scarce in cases of isolated fracture of the atlas Ordinarily they consist in pain and stiffness of the neck with tenderness, especially in the suboccipital area Motions are usually limited and slowly performed, though there may be instability causing the patient to hold his head with his hands⁷ Occasionally the patient may complain of tingling



Fig 1—*a* Anteroposterior view showing lateral displacement of both lateral masses of the atlas
b Lateral view showing fracture of both the anterior and the posterior arch of the atlas

and pain in the arms and legs despite absence of neurologic findings Swallowing may be painful or impaired because of retropharyngeal hemorrhage, particularly in cases of fracture of the anterior arch Involvement of the greater occipital nerve may produce neuralgia over its area of distribution Injury to a vertebral artery occurs in rare instances

In approximately 85 per cent of the cases one or both arches are fractured Plaut^{8, 9} has reviewed in detail the roentgenographic studies of these fractures The lateral view readily demonstrates fractures of the posterior arch (Figs 1b, 2 and 3) and may show a displaced fragment of the anterior arch (Fig 4) The anteroposterior view may show a gap in the anterior arch as well as an outward displacement of the lateral masses (Fig 1a) Fractures of the lateral masses are rare, only eight cases in all having been reported Even more rare are fractures of the transverse processes, the only reason that these are of clinical interest is that the fragments may injure a vertebral artery There are other roentgenologic signs of significance Swelling of soft tissue in the prevertebral space may mean fracture of the anterior arch¹⁰, an increase of the distance between the anterior arch and

the odontoid process may indicate rupture of the transverse ligament or dislocation

It may occasionally be difficult to rule out a congenital anomaly of the atlas Brown¹¹ reported a case of complete absence of the posterior arch Lawrence and Anderson¹² and Plaut¹³ reported a case of an anomaly of the posterior arch simulating a fracture and discussed differential diagnosis They noted a defect of one-half inch (1.3 cm) on each side between the pos-



FIG 2—Lateral view showing fracture and separation of the posterior arch of the atlas

terior arch and lateral masses, the posterior arch was in its normal position, the margins of the defect were smooth and there were neither small fragments of bone nor callus formation in the gap The infrequency of such anomalies permits them to be only rarely a source of confusion

Associated injuries frequently, in themselves, produce such overshadowing symptoms and signs that a fracture of the atlas may be overlooked and often they require immediate attention because of their own serious import In cases of such injuries the possibility of a fracture of the atlas should be kept in mind They most commonly include fractures of the odontoid process, of other cervical vertebrae and of the skull Complications most often encountered with fracture of the atlas are rotary subluxation, neuralgia of the greater occipital nerve and rupture of a vertebral artery—the vertebral groove having already been mentioned as a frequent site of fracture Transient pain and tingling in the arms and legs may be due to jamming of the medulla or cord, actual traumatic myelitis is rare

The differential diagnosis is not usually difficult Congenital anomalies have already been discussed Infections of the atlas are rare and are usually

of syphilitic or tuberculous type; they can be differentiated by history, general examination and laboratory and roentgenographic findings. This is true also of metastatic carcinoma. Arthritis of the upper cervical vertebrae may at times be indistinguishable from an old fracture, particularly if a history of injury is elicited. Roentgenographic studies of the atlas should be made in cases of occipital neuralgia, particularly those in which there is any history of trauma.¹⁴

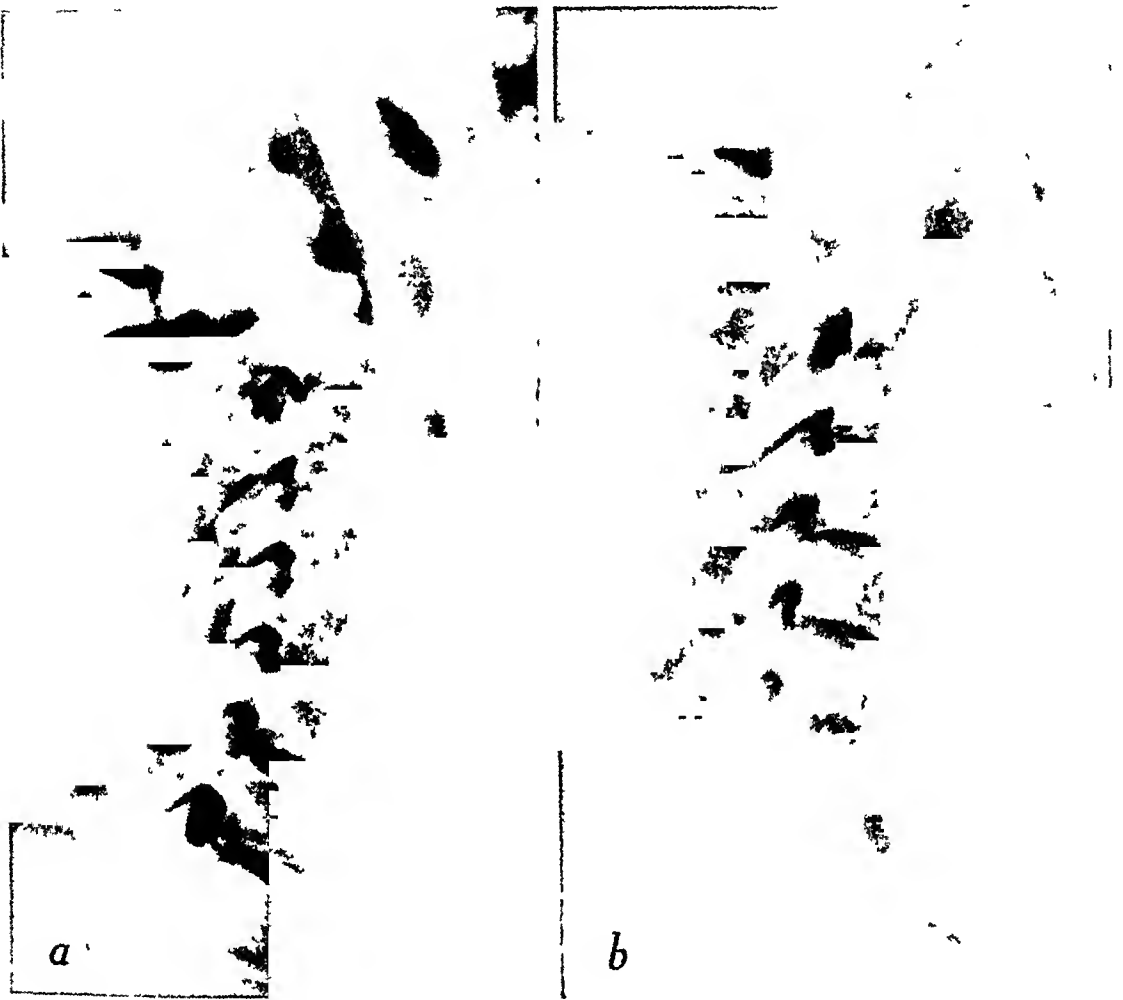


FIG 3—*a* Lateral view showing fracture of the posterior arch of the atlas and of the laminae of the second cervical vertebra and dislocation of the bodies of the second and third cervical vertebrae. *b* Three months later, showing some callus formation of the posterior arch of the atlas and partial reduction of the second cervical vertebra.

Treatment of fractures of the atlas has become fairly well standardized, good results have been obtained with most means used. Four to six pounds (1.8 to 2.7 Kg) of head traction in bed, in straight extension, is usually sufficient for immediate relief of symptoms, though occasionally more is needed. A Sayre sling will suffice for this. Relaxation of neck muscles is quickly obtained and in a few days a plaster encasement or a leather collar may be applied to immobilize the neck. Should the fracture be complicated by a tendency to sublunate, the traction may have to be continued for three to four weeks before use of a collar. Six to eight weeks after uncomplicated injury the patient is reexamined and new roentgenograms are taken. The collar is discarded at any time from eight weeks to four months, depending

on the progress of the patient and the roentgenographic findings. After removal of the collar, return of function is materially aided by physical therapy. Stiffness and limited motion of the neck are stubborn residua of such injuries. Though it may require some months, ultimate return of function is almost always complete. When complicated by greater occipital neuralgia, however, persistent pain may require surgical intervention. Lack

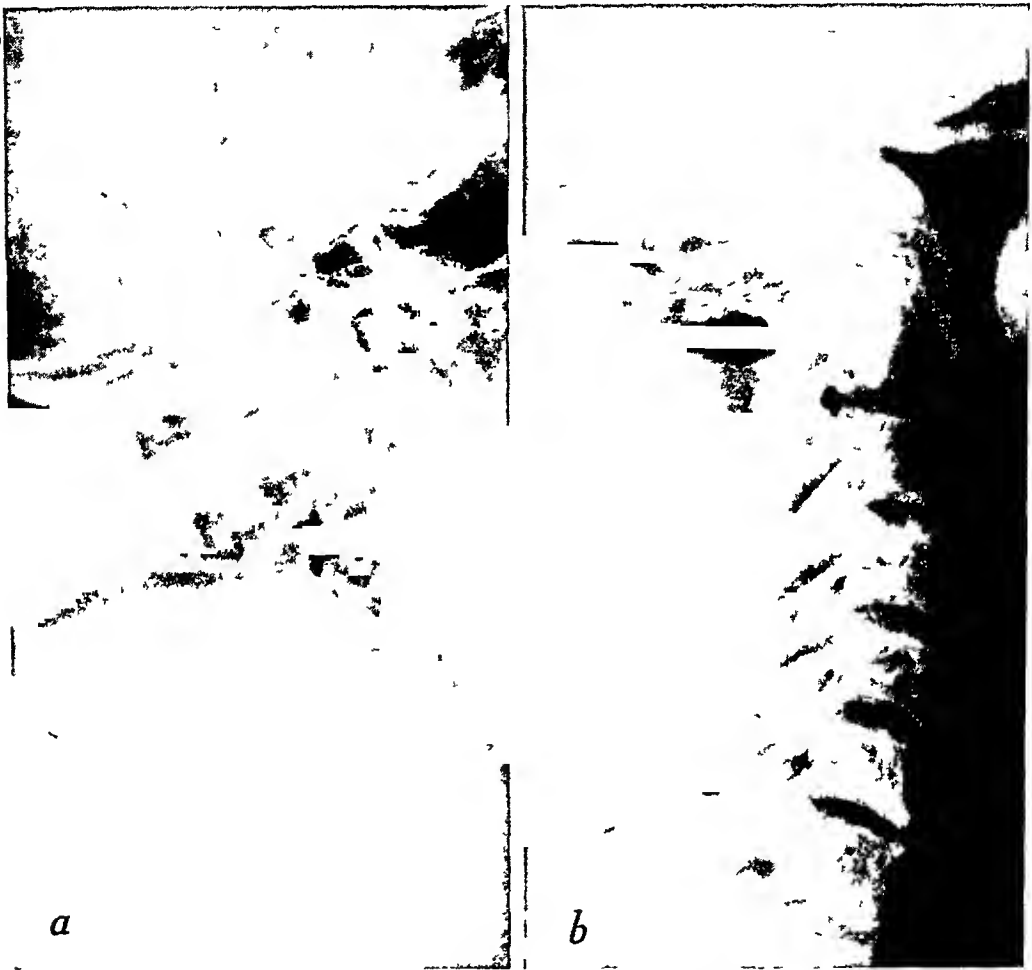


FIG 4—*a* Lateral view showing comminuted fractures with displacement of the anterior and posterior arches of the atlas. *b* Two and one half months later. Position slightly improved and some callus formation.

of callus formation is characteristic (Figs 3*b* and 4*b*), delayed or incomplete union occurring regularly and nonunion frequently.

Data on the eight cases encountered at the Mayo Clinic are summarized in Table I. The patients were evenly divided as to sex, ages ranged from 16 to 63 years. Trauma consisted of falls on head, blows on head, collisions and twisting of the neck under water as previously mentioned. There were six isolated fractures of the atlas, in one case a fracture of the second right rib was associated, and in the other a fracture of the laminae of the axis with a dislocation of the axis forward on the third cervical vertebra. The posterior arch alone was fractured in five cases, the posterior and anterior

arches were fractured in two and the articular facet was fractured in the remaining case. Treatment included various combinations of traction, rest in bed, encasement and collars are shown in Table I.

Results were classed as excellent if there was no limitation of motion of the neck, grating, pain or other disability and in three cases the results are so reported. Good results include one patient who noted slight limitation of rotation to the right and one patient who noted some limitation in rotation to both right and left. In two cases the results are classed as fair. In both of these there were slight tenderness to pressure over the back of the neck.

TABLE I
DATA IN CASES OF FRACTURE OF THE ATLAS

Case	Age, Years	Sex	Trauma	Fracture Site	Complications	Therapy	Results and Time
1	48	F	Turned head while under water	Articular facet	None	Collar	Excellent 12 years
2	16	F	Dived into shallow water hit top of head	Anterior and posterior arches	None	Traction and encasement	Excellent 14 years
3	35	M	Train collision	Posterior arch	None	In bed encasement	Good 22 years
4	58	F	Car collision	Posterior arch	None	Kept in bed	Good 23 years
5	28	M	Fell 55 feet (17 meters)	Posterior arch	None	In bed, encasement	Fair 16 months
6	63	M	Fell off load of hay on head	Posterior arch	None	Traction encasement	Poor 16 months
7	21	F	Car collision	Posterior arch	Fractured laminae of axis, dislocated axis anteriorly on third cervical vertebra	Traction, collar	Excellent 7 years
8	58	M	Fell 20 feet (6 meters)	Anterior and posterior arches	Fractured second right rib	Traction, encasement, collar	Fair 16 months

and limited rotation 16 months after injury, no further follow-up could be obtained. One patient complained of pain, grating and 50 per cent limitation of motion 16 months after injury and the result is classified as poor. It should be pointed out that the fair and poor results are in cases in which the follow-up is 16 months. With continued use, physical therapy and time, these patients may be expected to improve. There were no deaths in this group.

SUMMARY

Fractures of the atlas have been discussed and data on eight additional cases presented. This type of fracture is dangerous but not necessarily fatal. It probably occurs more frequently than has been reported but is overlooked. The usual treatment consists of traction followed by application of a plaster encasement or a leather collar. In three cases the results were classed as excellent, in two, as good, in two, as fair and in one case as poor. These fractures rarely unite but there is rarely any ultimate disability, although stiffness and limited motion of the neck may persist for several months.

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CHEST WOUNDS IN BATTLE CASUALTIES

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IN A PERIOD of approximately nine weeks during the campaign in France and Belgium, an Evacuation Hospital gave surgical treatment to 5,124 patients, nearly all of whom were battle casualties. One hundred and fifty-seven, or 3 per cent, of these patients had wounds of the chest cavity. There were 25 deaths, a mortality of 15.9 per cent. Six casualties, who died before reaching the operating room, are not included in this report.

In the 1914-1918 war, there were 4,595 cases of thoracic injuries among the American casualties, with a mortality of 24.05 per cent.¹ Gordon-Watson² states that the total mortality for chest wounds in the British Army in France, during the same war, was 27.5 per cent, and Brunner³ states that 2.6 per cent of all German casualties who reached casualty clearing stations had chest wounds. Holman⁴ estimates the mortality of chest cavity wounds, in the Pacific combat area, during this war, to be approximately 40 per cent.

Simple Hemothorax—Forty-five casualties had relatively minor penetrating wounds which caused simple hemothorax and required no treatment other than aspiration.^{5,6} In 12 of the 45 cases, the hemothorax was small and caused no respiratory distress, these casualties were evacuated without aspiration.

One patient, a prisoner of war, with a simple hemothorax died following a débridement of minor chest wall and arm wounds under sodium pentothal anesthesia. This patient had 800 cc of blood removed from the pleural cavity on admission, and a roentgenogram of the chest ten hours later revealed only a small amount of fluid. Immediately after operation, the patient developed acute respiratory distress and died within an hour. Autopsy showed the left chest to be filled with blood. It was not determined whether the bleeding had come from the lung or from an intercostal vessel. Whatever the source, it was presumed that the bleeding which had temporarily stopped was reactivated by the operative procedure.

Penetrating Wounds—Not Sucking—Forty casualties had penetrating wounds, not of the sucking type, with damage to the chest wall of such extent that serious injury to the lung was suspected. Limited thoracotomy was done in these cases, the chest being opened through the wound of entrance. In 23, a laceration of the underlying lung was found and sutured. The one death in this group occurred during the operation, when the lung was temporarily allowed to collapse to facilitate exploration of the chest cavity. The heart stopped suddenly and without warning, and all efforts to restore action were without avail.

Sucking Wounds—Thirty casualties reached the operating room with sucking wounds, but in every case the sucking had been temporarily controlled,

though not always completely, by dressings. A lacerated lung was found in 14 of these cases. The wounds of the chest wall were treated by a débridement, which included resection of all fractured rib ends. The opening in the chest cavity was then made large enough to allow satisfactory inspection of the lung and pleural cavity.⁷ Any lacerations found were sutured. No difficulty was encountered in closing the defect in the chest wall. In this group of 30 cases there were ten deaths, a mortality of 33.3 per cent. Gordon-Watson² in a review of 3,521 penetrating wounds of the chest, gives the mortality of sucking wounds as 44.6 per cent.

Deaths—1 The first death occurred in a soldier who had lost a large amount of blood and, at operation, was found to be bleeding from an intercostal vessel and a lacerated lung. The bleeding was controlled without difficulty, but only two pints of blood were available at the time to replace the massive blood loss. This amount was inadequate and, although he received continuous plasma and saline infusions, the patient died one hour after completion of the operation.

2 The second death occurred in a casualty who had a sucking wound and extensive damage to the lower lobe of the left lung. The lung was sutured and the chest wall closed. This patient died on the third postoperative day. Autopsy revealed a large amount of interstitial hemorrhage in the left lung but otherwise no satisfactory explanation as to the cause of death.

3 The third death occurred in a soldier with a sucking wound of the left chest and a laceration of the lung. He did not fully react following the operation, and died about eight hours after leaving the operating room. He had marked respiratory distress for which no adequate explanation was found at autopsy. There was a large congenital hernia of the left diaphragm which contained a part of the stomach, and this may very well have been a factor in the production of respiratory embarrassment.

4 The fourth death occurred in a soldier with two small sucking wounds of the left chest which were closed under local anesthesia. In this case, there was no laceration of the lung. This patient's major wound was a fractured jaw which bled freely and blood had been aspirated into the lungs. The patient developed a pneumonia which proved fatal on the first postoperative day.

5 The fifth death occurred in a soldier with a sucking wound of the right chest and a transection of the spinal cord at the level of the 11th thoracic vertebra caused by the same bullet. The patient died from pneumonia on the first postoperative day.

6 The sixth death occurred in a soldier with a sucking chest wound and a partial transection of the spinal cord at the level of the 4th thoracic vertebra. The sucking wound was closed and a laminectomy was done to explore the spinal cord. Death was caused by pneumonia.

7 The seventh death occurred in a prisoner of war with a sucking wound of the chest and a large laceration of the lung. The patient

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died on the first postoperative day. Autopsy revealed an extensive bronchopneumonia throughout both lungs.

8 The eighth death occurred in a soldier with a deep and irregular laceration of the right lung. This patient developed pulmonary edema and died on the first postoperative day. At autopsy, the damaged lung was found to be consolidated with blood which filled the bronchioles, alveoli, and interstitial spaces.

9 The ninth death occurred in an officer with an extensive wound of the chest wall and multiple deep lacerations of the lung, which were sutured with some difficulty. The patient died on the third postoperative day and, as in the preceding case, the principal finding at autopsy was a heavy consolidated lung filled with blood.

10 The tenth death occurred in a soldier with a large sucking wound of the right anterior chest and a complete fracture through the lower third of the sternum. There was little improvement in the patient's respiratory distress following closure of the wound. The mechanical difficulty of adequate respiration with a mobile lower sternum appeared to be the cause of death.

Tension Pneumothorax—Three patients were operated upon because of persistent tension pneumothorax. One had had his initial treatment at a Field Hospital, where a sucking wound had been closed. He was in acute respiratory distress on admission to the Evacuation Hospital two days later, and the right chest cavity was filled with air under pressure. At operation, a laceration of the right lower lobe was found from which air escaped with each respiration. The lung was sutured and the patient recovered.

The second tension pneumothorax occurred in a patient to whom we had given the primary treatment. There was an unrecognized depression of a fractured rib which caused a laceration of the lung, with resulting tension pneumothorax. The patient was returned to the operating room and the fractured rib ends were resected and the laceration of the lung sutured, following which the patient made an uneventful recovery.

The third tension pneumothorax occurred in a soldier who had had a sucking wound of the left chest closed at a Field Hospital three days before, and was in acute respiratory distress upon admission to our hospital. A thoracotomy was done, and the left lung was found collapsed. A laceration was sutured and the lung expanded, but the patient died at the end of the operation. Autopsy revealed considerable pneumonia in the lung of the opposite side.

Secondary Hemorrhage—One casualty developed a secondary hemorrhage ten days after being wounded. In this soldier, a bullet had entered the left shoulder, traversed the lung, and lodged in the 10th thoracic vertebra, causing a paraplegia. Although a fairly large hemothorax was present, it caused few symptoms, and was easily controlled by aspiration. Because of an alarming hemorrhage which occurred on the tenth hospital day, a thoracotomy was done. To control the bleeding, it was necessary to place a tourniquet around the hilus of the lung. The patient's condition was poor,

but there appeared to be no way to control the hemorrhage except by pneumonectomy. This was done, and he made a satisfactory recovery. Two weeks after operation he was transferred to a General Hospital, and a report ten days later stated that his condition was good. There was, however, no improvement in the paraplegia.

Thoraco-abdominal Wounds—There were 36 patients in this group. One patient died during the induction of anesthesia, and only 35 were actually operated upon.

Nineteen of the thoraco-abdominal wounds were on the right side and 17 on the left. In 11 cases it was possible to do an adequate, but not complete, abdominal exploration by enlarging the thoracotomy incision. When a complete abdominal exploration was needed, a celiotomy incision was necessary. The patients who had the chest pathology corrected prior to celiotomy did much better than those who had a celiotomy first. There were 11 deaths in this group, one preoperative and ten postoperative. In eight of these, death appeared to be due primarily to the abdominal injuries. One patient in the group died of an associated head injury.

Deaths—1 The first death occurred in a soldier with a penetrating wound over the liver and a small wound of the right chest caused by separate shell fragments. The operation was undertaken because of the injury to the liver and no operation on the chest was contemplated. This patient died during the induction of anesthesia and in addition to the laceration of the liver. Autopsy revealed a small hemothorax. There was no injury to the diaphragm and it is questionable whether this case should be included with the thoraco-abdominal wounds.

2 The second death occurred in an officer with a sucking wound of the left chest and an extensive laceration of the left kidney. The chest wound was closed and the kidney removed through an abdominal incision. This patient died on the seventh postoperative day of renal failure, with uremia. Autopsy revealed an atrophic, nonfunctioning right kidney.

3 The third death occurred in an officer who had severe wounds of the chest and abdomen. Through an abdominal incision, a laceration of the liver was sutured, and perforations of the stomach and colon closed. The chest wound, which was not the sucking type, was débrided and closed. This officer died on the fifth postoperative day. Autopsy revealed a large amount of blood in the pericardium although no penetrating wound of the pericardium or heart could be demonstrated. Some degree of tamponade had undoubtedly occurred, and it was felt that this was the primary cause of death.

4 The fourth death occurred in a soldier with a sucking chest wound and severe lacerations of the kidney and spleen. The patient was almost exsanguinated on admission to the shock ward. Operation was undertaken to control the bleeding but the shock was irreversible, and the patient died 12 hours after removal of the spleen and kidney.

5 The fifth death occurred in a soldier with a minor chest wound but with multiple perforations of the stomach, colon, and small bowel. At opera-

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tion, the peritoneal cavity was found to be filled with blood and intestinal contents. Death occurred on the day of operation due to shock and peritoneal infection.

6 The sixth death occurred in an officer with a large sucking wound of the chest, a perforation of the stomach, and a compound fracture of the humerus. The chest wound was closed and the fractured arm immobilized, but the patient continued in such poor condition that a celiotomy could not be undertaken. He died of shock and peritonitis.

7 The seventh death occurred in a soldier with a sucking chest wound and a severely lacerated liver. The chest wound was closed, and the liver packed through an abdominal incision. This controlled the bleeding but the patient died from shock on the first postoperative day.

8 The eighth death occurred in a soldier with a severe penetrating wound of the skull, a perforation of the colon, and a small sucking chest wound. All these wounds were given surgical treatment and the patient sent to the ward in fair condition. He died one week later from the intracranial injury.

9 The ninth death occurred in a soldier with a small chest wound, a laceration of the stomach and multiple perforations of the small bowel. Death was due to peritonitis.

10 The tenth death occurred in a prisoner of war, with a small sucking wound of the chest, lacerations of the spleen and kidney, a transection of the colon and multiple perforations of the small bowel. This patient died on the second postoperative day of shock.

11 The eleventh death occurred in a soldier with a large sucking wound of the chest and perforations of the small bowel. Closure of the sucking wound did not improve the patient's condition enough to permit celiotomy and he died of shock and peritonitis the day after admission.

Wounds of the Heart and Pericardium—Four patients were found to have wounds of the heart or pericardium. Two of the patients had lacerations of the pericardium without any damage to the heart. These lacerations were partially sutured and left so that the pericardial and pleural spaces were continuous. Both patients made uncomplicated recoveries. A third patient was found to have an hemopericardium of about 200 cc in addition to a sucking chest wound. The hemopericardium was suspected prior to operation as a splash could be heard with each heart beat. A small incision was made in the pericardium and the blood evacuated. The bleeding apparently had stopped, and its source was not obvious. The patient made a good recovery. A fourth patient with a sucking chest wound was found to have a laceration of the left ventricle. This patient died of hemorrhage as an attempt was being made to suture the laceration.

Crush Injury of the Chest—There was one crush injury in the series. This was caused by the wheel of a 2 5-ton truck passing over a soldier's chest, fracturing five ribs along the right anterior axillary line. The pain was so severe that breathing was entirely diaphragmatic, and a moderate degree of cyanosis was present. Under local anesthesia, the ends of the fractured ribs

were resected, and under one of the fractures a small tear in the pleura was found. Following operation, there was definite improvement in the respiration, and the soldier made an uneventful recovery.

Infection—All penetrating wounds of the chest wall, with a single exception were debrided, treated with penicillin and sulfanilamide, and completely sutured. In addition to local sulfanilamide and penicillin powder, all chest casualties received one gram of sulfadiazine every four hours by mouth, usually for a period of about seven days, and 20,000 units of penicillin intramuscularly every four hours for 48 hours. There were no wound infections and no infection of the pleural cavity during the period of observation, which was ten days to two weeks.

The one wound not completely sutured was in a prisoner of war whose wounds were two days old on admission, and badly infected. There were multiple wounds of the chest wall, two had penetrated the chest cavity, and one shell fragment had perforated the diaphragm. In this case, the wounds of the chest wall were débrided and the muscular layer closed, but the skin was left open. The pleural and peritoneal cavities were grossly contaminated but they did not at any time present evidence of an active infection. The patient was evacuated on his tenth postoperative day in excellent condition.

Foreign Bodies—No patients were subjected to operation solely because of the presence of a foreign body in the chest cavity^{7,9}. In eight cases, however, foreign bodies were removed, six were in the periphery of the lung and two were free in the pleural cavity.

Drainage of Chest Wounds—The pleural cavity was not drained following any of the III operative procedures. One or more aspirations were usually needed before the patient was evacuated. One patient, with a thoraco-abdominal wound of the right side, collected a large amount of bile in the right chest. This was controlled by daily aspiration, and the drainage had almost stopped when the patient was evacuated on his twelfth postoperative day.

CONCLUSIONS

Experience based upon the relatively small number of cases in each group does not justify fixed conclusions as to treatment but does offer suggestions.

1 Small penetrating wounds of the chest cavity causing simple hemothorax are best treated by aspiration alone.

2 Penetrating wounds of the chest cavity, with fractured ribs or suspected injury to the lung, should have a limited thoracotomy through the wound of entrance or exit. The fractured rib ends should be resected, the blood evacuated, and the lacerations of the lung sutured.

3 In treating sucking wounds of the chest, an incision large enough to allow inspection of the lung is usually indicated because of the probability of lung injury. A laceration which leaks air or bleeds is often found and should be sutured.

4 Thoraco-abdominal wounds are usually best handled by two incisions.

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TABLE I

		Deaths	Mortality
Wounds of chest cavity	157	25	15.9%
Operative procedures	111	24	21.7%
Simple hemothorax	45	1	2.2%
Penetrating wounds	40	1	2.5%
Sucking wounds	30	10	33.3%
Thoraco-abdominal wounds	36	11	30.5%
Wounds of heart and pericardium	4	1	25.0%
Crush injury	1	0	0
Tension pneumothorax	3	1	33.3%
Secondary hemorrhage	1	0	0

In 23, or 57.5 per cent, of the penetrating wounds, and in 14, or 46.6 per cent, of the sucking wounds, lacerations of the lung were found and sutured.

Three patients with wounds of the heart and pericardium are also classified with the sucking wounds.

Two patients developed tension pneumothorax after closure of sucking wounds, and in the third, tension pneumothorax developed in a patient with a penetrating injury which had fractured and depressed a rib. Classified separately for emphasis.

In most cases the thoracotomy should be done first and then the celiotomy.

5 The ends of fractured ribs, particularly when it is suspected that a piece of rib may penetrate the pleura, should be resected. Local anesthesia is the anesthesia of choice for this procedure.

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THE PROBLEM OF MASSIVE HEMORRHAGE FROM DUODENAL ULCERS OF PATIENTS BEYOND MIDDLE LIFE

WITH PARTICULAR REFERENCE TO THE VALUE OF THE DEVINE EXCLUSION
OPERATION IN SELECTED CASES OF THIS NATURE

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CONSIDERING both the acute massive and the chronic types of hemorrhage, most authors are agreed that about 25 per cent of patients suffering from duodenal ulcer are subject to this complication. In cases in which the patients are less than 45 years of age, it is a serious but usually not fatal complication, for conservative measures usually suffice to control the bleeding. However, if the patient is 45 years of age, or more this bleeding becomes much more ominous. Allen and Benedict,² Bohier,³ Westermann,⁹ and many others, have emphasized that half of these older patients beyond age 50, who have bled have had the massive type of hemorrhage and that about a third of these patients will die of hemorrhage if treated conservatively and supportively.

Whether or not surgical treatment is logical for this 33 per cent of patients more than fifty years of age who may die otherwise is still hotly contested and a tremendous literature has grown up about the subject. As greater numbers of these patients are operated upon, and as surgical technic and post-operative care are perfected, those operations giving poor results should be eliminated. Furthermore, the immediate mortality rate should decrease. Walters and Cleveland⁸ have compared the risk of partial gastrectomy for bleeding peptic ulcer in 135 cases in the five-year period ending with 1936, with that of 119 cases in which operation was performed in 1940. In the earlier group the mortality rate was 10 per cent, in the latter group, 4 per cent. The time of operation and the type of procedure were found to be important, considering the age and condition of the patient.

Finsterer⁶ has urged immediate operation during the acute phase of the bleeding. He reported data on a series of 78 cases in which operation was performed within 48 hours of the massive hemorrhage. Four patients died (5 per cent). Gastric resection was performed in 71 cases and gastro-enterostomy in seven. In a series of 74 cases in which operation was not immediate, 22 patients died (30 per cent). Large enough series of such cases still have not been reported to enable one to draw final conclusions.

A decision as to the type of procedure to be performed is difficult to reach. Gastric resection with removal of the hemorrhagic lesion should be the opera-

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tion of choice. In any event, all the mucous membrane of the pyloric antrum should be removed whenever at all possible. In a recent study by us, recurrence of gastrojejunal ulceration or bleeding occurred in from 10 to 16 per cent of cases after the Finsterer type of resection, in about 40 per cent of cases after the Devine exclusion operation and in more than 60 per cent of cases after the Eiselsberg operation, in all of which varying amounts of pyloric antrum are left. Walters and Cleveland reported 92 per cent satisfactory results following partial gastrectomy for bleeding peptic ulcer if the pyloric antrum was removed and if entero-anastomosis was not performed. In the 112 cases followed by these authors there were 15 unsatisfactory results. In four of these 15 (27 per cent), the pyloric sphincter and antrum were not removed. In one of these four cases death occurred from massive hemorrhage four years later. For bleeding duodenal ulcer alone, they reported 94 per cent satisfactory results following partial gastrectomy. Only two of these patients failed to obtain relief from primary gastric resection and in both cases the antrum was not removed.

The importance of removing the pyloric antrum and pyloric sphincter cannot be overemphasized, but it was not until recently that this fact has been appreciated thoroughly. The recent study by us of all types of exclusion operations, whether or not resection was performed, demonstrated this point clearly. The pyloric antrum should be removed to give the patient the best chance of permanent cure. The study, likewise, emphasized, however, that in many cases the condition of the patient is too poor to justify extensive gastric resection and that in many cases the duodenal lesion is the site of too active inflammation, hemorrhage and edema to warrant the extensive dissection necessary to include the antrum. Whether or not the antrum is to be included in the resection in such cases must be decided by the surgeon. Rarely it may happen that not only is the possibility of resecting the antrum remote but the patient is in such poor condition that resection of any kind is foolhardy. This is particularly true of bleeding lesions of elderly patients. Since Finsterer,^{6,7} Allen,¹ and others have emphasized the necessity of removing at least two-thirds of the stomach if resection is undertaken, removal of lesser amounts of the stomach to decrease the risk in cases in which the patients are very ill gains little. Yet the patients must be protected as well as possible against further hemorrhage. It was this particular problem that led to a further study of the various exclusion operations.

The ideal operation for these elderly patients who have experienced massive hemorrhage should be performed quickly and easily, with as little trauma as possible because of their hemorrhagic tendency. It should allow complete isolation, the exclusion of the ulcer from the gastro-intestinal continuity, since these people, as a rule, are too ill to allow direct attack upon the point of bleeding by the radical expedient of gastric resection. The Devine exclusion operation meets these requirements, but recurrence of trouble was noted in about 40 per cent of the 62 cases studied by us. It will be noted, however, that only a relatively small percentage of these patients were more than 50 years of age at the time the exclusion operation was done.

Devine^{4, 5} first employed his exclusion operation in 1916, and recommended it for use if the patient was a woman, in cases of cicatricial, stenosing ulcer, and in cases in which the lesion was deep on the posterior duodenal wall. He expressed the belief that the number of good results compared favorably with the results of gastric resection, without the risk of the latter. He simply transected the stomach at the angle, though he believed that the closer to the cardia the division was made, the greater the resulting achlorhydria. The pyloric segment was closed and retrocolic, complete, termino-lateral gastrojejunostomy was performed. The operation obviously is much quicker and simpler than any resection. The storm of controversy aroused concerning this operation is reflected in the voluminous literature that has accumulated. The consensus of surgeons seems to be that in most cases of duodenal ulcer there is no place for treatment by a Devine exclusion operation.

ANALYSIS OF DATA FROM THE MAYO CLINIC

Data on 62 patients upon whom the Devine exclusion operation was performed at the Mayo Clinic in the 15-year period ending January 1, 1941, form the basis of this particular study. This is the same group of patients followed by us in our study of all exclusion operations performed at the clinic in that period. It may be that the Devine exclusion operation will find its only use in carefully selected cases in which the patients are 50 years of age, or more, have severely bleeding duodenal lesions and are in poor condition for any surgical procedure.

Of these 62 patients, three died in the hospital, a mortality rate of 5 per cent. Only one of the three was more than 50 years of age. He was a 52-year-old man, for whom gastro-enterostomy had been performed years before, because of a severely bleeding duodenal ulcer. He had had at least three episodes of bleeding between the two operations. He was severely anemic and in poor condition at the time of operation. A subacutely inflamed duodenal lesion was found. The patient died seven days after operation as the result of intestinal obstruction. Thirty-six of the entire group (58 per cent) were found at operation to have either a subacute or an hemorrhagic lesion. Seventeen of the group were 50 years of age, or more, and only one (6 per cent) of these died after operation, in spite of the fact that all but two were in poor condition for any operation.

Of the 59 patients who survived operation, 52 were traced carefully. Follow-up studies of patients who have had operations upon the stomach are eminently unsatisfactory. There is no period of years which can be set arbitrarily, beyond which, if the patient has remained well during that period, he may be assured of a permanently good result. As of November 1, 1941, 21 patients (40 per cent) were known to have had further trouble, manifested by hemorrhage, necessitating further operation, or had been proved by roentgenologic examination to have had stomal ulceration. A study of these 21 poor results is interesting.

Fifteen of the 21 patients who had recurrence of trouble were less than

50 years of age. Three only (14 per cent) of this unfortunate group were 50 years of age or more. All three had had acute bleeding, and all had had previous operations for the ulcer. A man, age 59, had had episodes of severe bleeding from a proved duodenal ulcer. At the age of 54 he had had a perforation of a "peptic" ulcer, which was closed simply. His condition was unfavorable for surgical treatment, and at operation it was impossible to perform retrocolic anastomosis of any kind. A Devine exclusion operation and antecolic, complete (Pólya), terminolateral gastrojejunostomy were done. An entero-anastomosis was made. This case has been quoted by Walters and Cleveland also. The patient had a severe hemorrhage within two months, another in eight months, and he died of hemorrhage 15 months after the operation. Walters and Cleveland as a result of study of such cases, have mentioned the inadvisability of performing entero-anastomosis when dealing with a bleeding duodenal lesion.

In the second of these three cases the patient was a woman age 58. She had a history of bleeding duodenal ulcer of many years' duration. Twenty years previously a perforation of the ulcer had been closed. Seven years previously gastro-enterostomy for bleeding duodenal ulcer had been done. At operation, she was observed to have a subacutely inflamed duodenal ulcer with much brawny edema. Her immediate course was good but further trouble developed in six months, and reoperation was performed several times for gastrojejunal ulceration. The patient finally died after one of these operations.

In the third case the result must be listed as poor, although the patient is living and well five years after the Devine exclusion operation. He was a man age 56 and also had a history of acute hemorrhage from a duodenal ulcer. Posterior gastro-enterostomy had been done five years previously but the stoma had been disconnected because of a large gastrojejunal ulcer one year previous to the Devine exclusion. Soon after normal gastro-intestinal continuity had been reestablished, the ulcer became reactivated and bled on at least one occasion. The patient was in poor condition, being anemic and dehydrated. At operation, it was not thought that he could withstand an extensive procedure and the Devine exclusion operation was performed. He did very well for nearly two years but then returned to the clinic with typical symptoms of a gastrojejunal ulcer, without bleeding. This was proved by roentgenologic examination, and he was sent home on medical management. Three years later, or five years after the exclusion operation, he was much better, did not have any bleeding, and was quite active.

The remaining 31 patients of the 52 traced were found, as of November 1, 1941, to have had either no further trouble or only mild symptoms of indigestion. There was no bleeding, no further operation, and no proved gastrojejunal ulceration. Twenty-one of these patients were considered to have had good results and ten had had only fair results. Since this operation was performed more frequently in the early portion of the 15-year period than later, many of the patients have been followed ten years

or more. Only three (10 per cent) were traced less than three years, while 19 (61 per cent) were followed more than ten years and five (16 per cent) were traced 15 years or more.

As contrasted with the group of poor results, in which only 14 per cent of the patients were 50 years or older, in this group of 31 patients, 13 (42 per cent) were more than 50 years of age. Four of the patients were more than 60 years old. Eight had had episodes of massive hemorrhage, requiring transfusion, or attended by syncope and prostration. Four had had previous operations for the ulcer, two of the four had had multiple previous operations. All but two of these 13 patients were considered to be in poor condition at the time of operation but the risk of operation was thought to be less than the risk of exsanguination. In all, of the 62 patients studied, 17 were 50 years of age or older. One of these died (6 per cent) after operation. Thirteen (81 per cent) of the remaining 16 obtained good results.

The problem is illustrated by the two following reports of cases.

CASE REPORTS

Case 1—A white, male, farmer, age 53, was admitted to the Mayo Clinic July 25, 1928. He was obviously very ill. His familial history was noncontributory. He had been fairly well until the onset of his present illness and had not had any operations.

The patient complained that for about a year he had been having "stomach trouble." This was manifested by typical postprandial epigastric distress, usually relieved by food, sodium bicarbonate or belching. There was occasional vomiting but none of it was of retention character. The distress had become progressively worse with only short intervals of remission and on two occasions he had noted tarry stools followed by weakness and dizziness. No massive hematemesis was reported. During the six months prior to admission he had noticed extension of the epigastric pain to his back, and had complained of increasing weakness and dizziness.

In addition, the patient had been told 15 years previously, during a life insurance examination, that he had "heart trouble." For five or six years he had noticed exertional dyspnea but had not had any severe precordial pain. Tachycardia and palpitation were occasionally present. No orthopnea or edema of ankles or face had been observed.

On examination, the patient was markedly undernourished and anemic. The lungs were clear but the heart was enlarged, and a loud, rough, blowing systolic murmur was heard at the apex and transmitted to the axilla. There was no sign of myocardial failure. Blood pressure was 120/80, in the lying position. There was slight epigastric tenderness but no mass was felt. The prostate was enlarged and firm, and moderate sclerosis of the peripheral vessels was noted.

Urinalysis showed a small amount of albumin and an occasional leukocyte. The concentration of hemoglobin was only 17 per cent and the erythrocytes numbered 2,270,000. The blood urea value was normal. The flocculation reaction for syphilis was negative. Prostatitis and a small amount of prostatic obstruction were noted. The electrocardiogram showed sinus tachycardia and aberrant QRS complexes. Exaggerated P waves were present in lead II. A roentgenogram of the stomach showed an ulcer, with deformity of the second portion of the duodenum.

The patient's condition obviously was unfavorable for surgical treatment. He was thought to have chronic mitral endocarditis, well compensated. It was felt that he was probably bleeding from a perforating duodenal ulcer, and that operation should be performed.

MASSIVE DUODENAL HEMORRHAGE

At operation, August 2, 1928, a large inflammatory mass involving the first part of the duodenum was found. It had perforated into its surrounding omental tissues, with resulting edema and brawniness of these tissues. It was technically impossible to free up the duodenum and a Devine exclusion operation was performed. The stomach was divided at the angle, the pyloric end was closed and retrocolic, complete (Polya) gastrojejunostomy was done. The postoperative course was not complicated and the patient left the hospital on the fourteenth day after operation.

The patient returned to work within two months and, in answer to an inquiry, seven years later (1935) stated that he had not had any more bleeding. He did not make any complaints referable to his stomach at that time. In June, 1941, 13 years after the operation, he was still well. He still did not have any symptoms referable to the stomach, and had not had any further bleeding.

Case 2—A male Negro, age 60, was admitted to the clinic, August 11, 1928, complaining of "stomach trouble" of 30 years' duration. His family history was noncontributory. He had not had any serious illnesses or any previous operation.

The "indigestion and stomach trouble" were manifested by periodic attacks of postprandial epigastric distress lasting eight to ten days in the spring and fall, and controlled by food or sodium bicarbonate. The patient had never had adequate medical care. One and one-half years before admission he had had a severe attack during which he may have fainted. One month before being seen at the clinic he had vomited large quantities of coffee-ground material and had fainted. Tarry stools were present for about a week. Peptic ulcer had been diagnosed.

On examination, the man appeared anemic. His pupils reacted sluggishly to light but well to accommodation. There was a slight exudate over the right fundic field. Otherwise, the physical examination gave normal results.

The results of uranalysis were normal except for a few hyaline casts and a small number of leukocytes. The hemoglobin content of the blood was only 27 per cent of normal, and erythrocytes numbered 2,600,000. The flocculation reaction for syphilis was negative. Examination of the right fundus revealed moderate retinitis, probably associated with the anemia. A roentgenogram of the stomach revealed a duodenal ulcer.

At operation, August 16, 1928, a scar of an old ulcer was seen on the anterior duodenal wall. The scar was excised by cautery. This was not thought to be the source of the bleeding. There appeared to be a second lesion deep in the posterior wall of the duodenum, which had perforated onto the pancreas. Because of the repeated hemorrhages and the location of this deep lesion a Devine exclusion operation was performed. The stomach was divided above the angle, the pyloric half was closed and gastro-intestinal continuity was restored by retrocolic complete (Polya) gastrojejunostomy. The patient contracted pneumonia on the fifth postoperative day but finally recovered.

Since the operation the patient has been heard from on several occasions, last in June, 1941, 13 years after the exclusion operation. At no time has he had further bleeding. He has gained weight, but has multiple minor symptoms, none of which are referable to the stomach.

COMMENT.—After careful evaluation of the history and physical findings of these patients more than 50 years of age, who had bleeding duodenal lesions, it does not seem probable that any of them would have survived extensive gastric resection. Anything less than an extensive resection has been shown to give little better ultimate results than an exclusion operation or gastro-enterostomy. Furthermore, in none of these cases would it have been technically possible, or reasonably safe, to dissect the duodenum free enough to allow transection below the pylorus.

SUMMARY

Ample evidence has been accumulated to emphasize the necessity of resecting the pyloric sphincter and antrum whenever possible in the course of a high gastric resection for duodenal ulcer. There are, however, many instances in which surgical discretion forbids such an ideal procedure (1) because the duodenal lesion is the site of active inflammation and is surrounded with indurated and edematous tissue, or (2) because the patient himself is in no condition to undergo an extensive resection, or (3) for both reasons. The surgeon then must exercise judgment and perform that operation which seems indicated.

The Devine exclusion operation would seem to have only a limited place in the repertory of treatment for duodenal ulcer. Of a group of 62 patients of all ages, for whom the operation was undertaken, we succeeded in tracing 52. Forty per cent of the traced patients were known to have had recurrence of trouble. However, if the operation is to be performed at all, it would seem indicated only for that small and select group of elderly patients who have bleeding, nonobstructing duodenal lesions and who for various reasons are in poor condition for any type of surgical treatment. Seventeen patients age 50 years, or more, were found to be included in this group of 62. One of these patients died seven days after the operation (6 per cent). Of the remaining 16, only three (14 per cent) were included in the group of 21 who had recurrence of trouble. One of these three has since become well. Thirteen were part of the group of 31 (42 per cent) who obtained good results from the operation. While only 31 (60 per cent) of the 52 patients of all ages whom we succeeded in tracing obtained good results, 13 (81 per cent) of the 16 elderly patients have not had any further trouble. That they survived the operation at all is a good argument for its use in such cases.

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PANCREATICODUODENECTOMY FOR ISLET CARCINOMA*

A FIVE-YEAR FOLLOW-UP

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Case Report—Unit No 392089 Mrs A. C., age 53

History The patient was first studied in the Vanderbilt Clinic, in February, 1940, for a complaint of epigastric pain and loss of weight and strength of two month's duration. Her past history, except for three similar attacks 23, 12 and 5 years ago, was irrelevant. During the previous two months, as a result of excessive work, she had developed a severe burning epigastric pain, with acid eructations, relieved by alkalies and small feedings of bland food. During this time she had lost 12 pounds, and had an admission weight of 80.25 pounds. She was admitted to the Medical Service.

Physical Examination The patient was a tired, thin woman, looking chronically ill, not anemic or jaundiced. The only positive findings were in the abdomen. There was epigastric tenderness, high up near left costal margin and below and to the right, just above the umbilicus, could be felt a firm, nontender movable mass, four centimeters in diameter.

Laboratory Data Hb, 11/7 Gm, R. B. C. 4,100,000, normal white cell count and differential. Gastric analysis: Free HCl—O, 20 minutes after histamine—58. Guaiac test—negative. Urinalysis: No abnormalities.

Barium Meal 50% six-hour residue. A large filling defect was found in the pars media and antral portion of the stomach, which corresponded to a mass palpated in the epigastrium. On the lesser curvature, near the filling defect in the antrum, a persistent barium projection is seen, one centimeter in depth and diameter—characteristic of a penetrating ulcer.

She was observed on the Medical Ward for a week, where she was seen by the surgeons, and everyone agreed with the diagnosis of carcinoma of the antrum of the stomach, and she was, therefore, transferred to the Surgical Service.

Operative Report—Doctors Whipple and Nelson (March 6, 1940). Preoperative diagnosis: Carcinoma of the antrum. Postoperative diagnosis: Carcinoma of the head of the pancreas.

Partial gastrectomy, complete duodenectomy, removal of head and part of body of pancreas, anterior gastro-enterostomy, end-to-side, and choledocho-enterostomy.

Operative Pathology The findings in this patient proved to be quite unexpected. Because of the patient's symptoms, the presence of a movable mass and the positive roentgenologic diagnosis of a carcinoma of the antrum of the stomach, the patient was operated upon with the idea of partial gastrectomy. When the thin abdominal wall was opened the mass could be felt in what was thought to be the posterior wall of the stomach. Because it moved easily the lesser sac was not opened to inspect the posterior wall of the stomach. This was a mistake, for the mass, which proved to be a tumor of the head of the pancreas, was not discovered until after the stomach had been transected. However, the ultimate procedure was not materially endangered because the patient was not jaundiced, and it was felt that a one-stage procedure could be carried out in this case—and it was essential to do so, once having cut through the stomach. The tumor mass was found to be occupying the head of the pancreas. It was hard, but moved over the underlying structures, and no enlarged nodes were felt. When it was being dissected away

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from the portal vein and the superior mesenteric vessels, great care had to be taken because it was thought that in another two or three weeks it probably would have begun invading the vessels

Procedure A left rectus incision was made. When the tumor mass was felt freely movable on what was thought to be the posterior wall of the stomach, a resection was begun by ligating the vessels in the greater and lesser curvatures at the junction of the upper and middle thirds. The stomach was cut across between Payr clamps and the proximal one covered with a protecting pad, as was the distal one, and the stomach drawn to the right, when it was discovered that the tumor mass was not in the stomach but in the head of the pancreas. The common duct was found to be dilated, although the patient was not jaundiced, and the cystic duct had a somewhat abnormally long course, and it was doubtful as to whether or not the gallbladder could be used for anastomotic purposes.

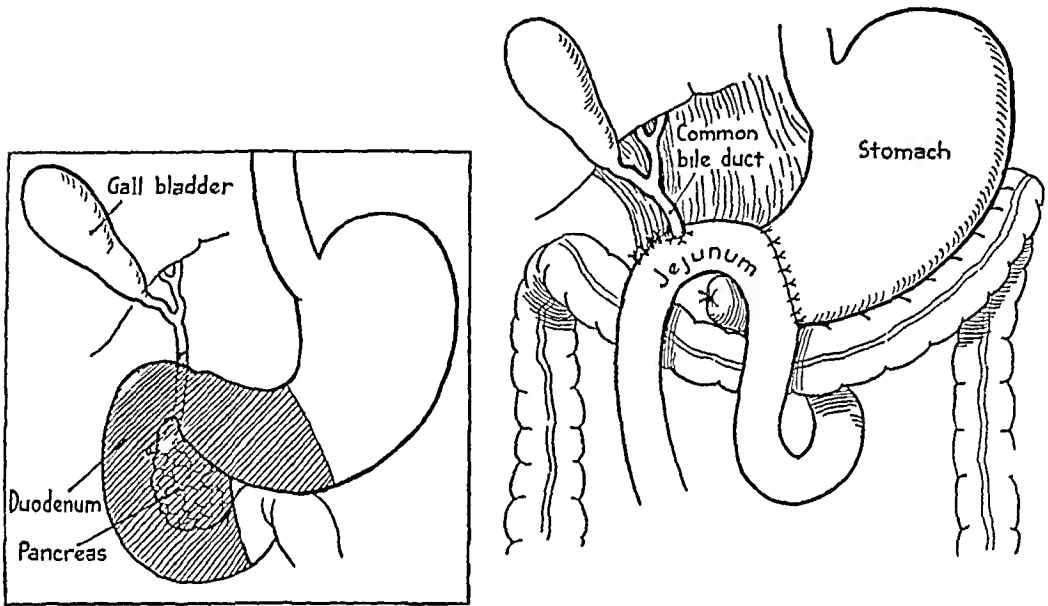


FIG. 1.—One stage radical pancreaticoduodenectomy, with antecolic gastrojejunostomy and implantation of the common duct into the jejunum

Inasmuch as the duct was dilated, it was decided to transplant it into the jejunum which would be used for the gastro-enterostomy. Furthermore, this made it easier to continue the dissection of the duodenum. The gastroduodenal artery was ligated, which controlled a good part of the arterial hemorrhage, and the dissection of the duodenum with the head of the pancreas was then begun.

The peritoneum to the outer side of the duodenum was incised, the duodenum mobilized, and the branches of the inferior pancreaticoduodenal artery ligated. The junction of the head and body was found to be narrow. It contained a dilated pancreatic duct which was ligated and the pancreas cut through. The junction of the duodenum and jejunum was then drawn to the right, behind the superior mesenteric vessels, and the duodenum cut between Payr clamps at the junction between the duodenum and jejunum. The distal cut end was then sutured with an over-and-over stitch of No. 00000 chromic and the stump was then buried with interrupted No. 1 silk mattress sutures. When the stump was released it passed behind the superior mesenteric vessels into the greater peritoneal cavity. With the freeing of the duodenum at this point the head of the pancreas was dissected away from the portal vein and splenic vein and from the superior mesenteric vessels. The patient did not lose much blood and the entire specimen of the distal half of the stomach and all of the duodenum and head of the pancreas and terminal

PANCREATICODUODENECTOMY

part of the common duct were removed. A loop of jejunum was then brought up in front of the colon and an antecolic gastrojejunostomy, end-to-side, was established between the cut end of the stomach and the antimesenteric border of the jejunum, beginning with a seroserosus suture of C silk. The clamp was removed from the stomach and the contents of the stomach aspirated. An incision in the jejunum corresponding in length to the cut end of the stomach was made and the stomata united by No 00000 chromic on two needles, beginning at the middle of the two adjacent parallel cut edges, locked at the angles and carried around to a point opposite the point of beginning, an over-and-over

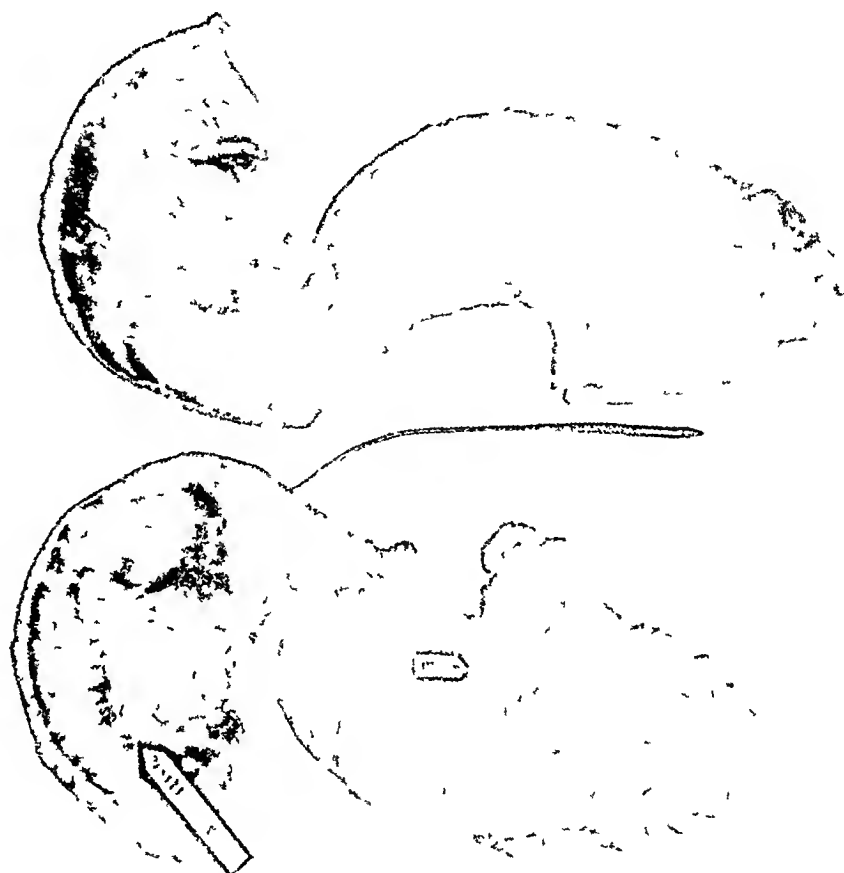


FIG 2—Gross section of the tumor and duodenum, with probe through the common duct and papilla of Vater

suture being used. The seroserosus suture was then carried to the point of beginning. Finally, the cut end of the common duct was opened by removing the Kocher clamp, the excess bile aspirated and the anastomosis between it and the jejunum distal to the gastrojejunostomy was carried out by a seroserosus suture of C silk. The opening in the common duct and an opening in the jejunum similar in diameter were united by an over-and-over suture of No 00000 chromic and the seroserosus suture carried around to the point of beginning. This completed the procedure. Hemostasis was found complete and the pad count reported correct. A Penrose tube was placed down to the bed of the pancreas.

Closure. Peritoneum and posterior rectus sheath with interrupted No 1 silk mattress sutures, anterior rectus sheath with far- and near-interrupted sutures of C silk, skin with interrupted silk.

Condition—remarkably good. **Medication**—slow transfusion. **Specimen**—distal half of stomach, all of duodenum, head of pancreas, and terminal part of common duct. **Drains**—one Penrose tube. **Case**—clean-contaminated. **Technic**—silk.

The pathologist reported the tumor as being a carcinoma of the head of the pancreas, but of the islet cells rather than the acinar tissue. In addition a penetrating benign ulcer on the lesser curvature of the stomach was found (Fig 2). Dr Stout's report is as

FIG 3

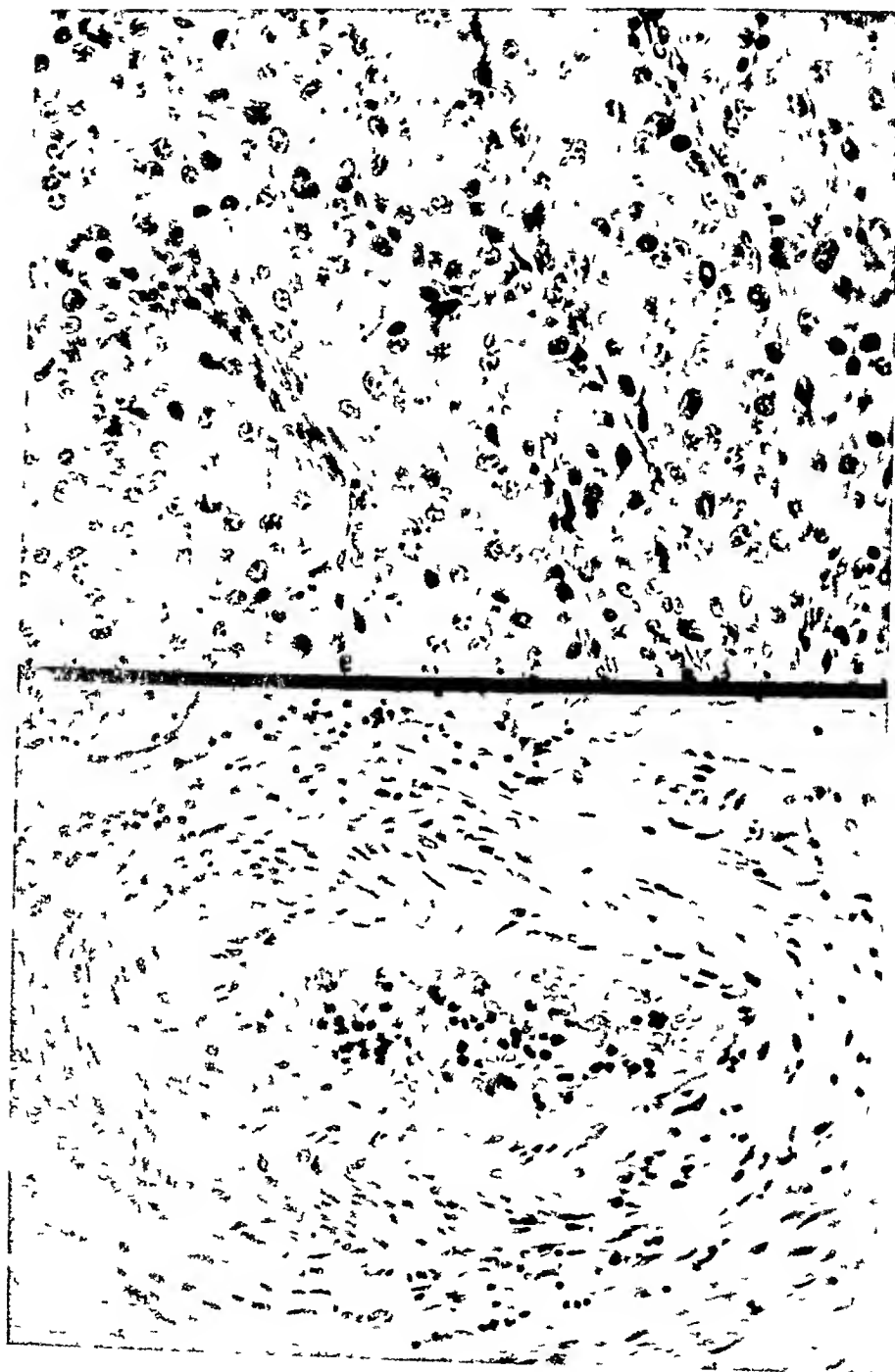


FIG 4

FIG 3—Microscopic picture of the islet cell tumor of the pancreas
FIG 4—Section of vessel showing islet cells in the lumen

follows "This appears to be a characteristic and well-differentiated tumor of islet cells. Most of the cells are filled with characteristic granules (Fig 3) and it is surprising that the patient did not show clinical symptoms of hyperinsulinism before operation. The tumor has infiltrated the head of the pancreas, destroying most of it. It has surrounded and infiltrated the wall of the common duct as it passed through the head of the pancreas, and in this way narrowed the lumen. It has infiltrated many large and small veins (Fig 4), so that the possibility of venous metastasis must be kept in mind. No lymph node metastases have been found in any of the lymph nodes examined. The remaining pancreatic tissue, except where it has been attacked by the tumor, is relatively normal in appearance and is well supplied with islets. The small ulcer high on the lesser curvature of the stomach has produced marked destruction of the muscular coat, although a few muscle bundles can still be noted in the scar tissue forming the bed of the ulcer." Dr Virginia Kneeland Frantz reported as follows "With Bensley's stain the granules all stain red. If the stain is reliable, which it has not been previously in our hands with human tissue, this would mean that the tumor is composed of *alpha* cells."

Fasting blood sugars after operation showed normal levels of 98 to 104 mg per cent.

Subsequent Course—The patient made an uneventful convalescence. She has been followed frequently in our Metabolism Clinic because of a fat indigestion. She shows from 30 to 50 per cent fat loss in her stools on repeated measured fat intake and output studies, but this fat loss in the stools is controlled somewhat by the use of 5 panteric and 9 holadin tablets o.d. Her weight is maintained at 90 to 94 pounds. She is still just as active and busy in her household duties and in work as a clergyman's wife in his parish as at any time before her operation. At no time has she shown any evidence of hyperinsulinism or of hypoglycemia either symptomatically or by fasting blood sugar determinations.

COMMENT This is the first recorded one-stage removal of the head of the pancreas and duodenum, with occlusion of the pancreas. Trimble reported a similar procedure, carried out independently in a patient operated upon several weeks later. As a result of our experience in some 27 radical pancreaticoduodenectomies, 22 for malignant neoplasm and 5 for calcification of the pancreas, we now advocate the one-stage procedure for the following reasons:

- 1 The danger of hemorrhage and postoperative oozing is controlled by preoperative vitamin K therapy.
- 2 The danger of two anesthetics and two major procedures is avoided.
- 3 The difficulties of extensive and in some cases massive adhesions at the second and more difficult stage are avoided.
- 4 Continuous spinal anesthesia, together with plasma and whole blood transfusion, has made the one-stage procedure safer than the two-stage procedure. We have performed eight two-stage operations, with a mortality of 38 per cent, whereas, in 19 one-stage operations our postoperative mortality from all causes was 31 per cent. We have lost no patients with one-stage procedures for benign lesions.
- 5 In the one-stage procedure we have found two steps of great advantage:
 - (a) The implanting of the common duct into the jejunum, either end-to-end or end-to-side, depending on the choice of the loop or Roux-type of jejunojejunostomy. This avoids the dangers of a cholecysto-

- enterostomy, and the serious complication of a biliary fistula as a result of the cutting through of the ligature on a ligated common duct
- (b) The implanting of the pancreatic duct into the jejunal loop below the choledochojejunostomy. This eliminates all the uncertainty and debate regarding an occluded pancreas and possible fatty liver degeneration

There have been many modifications of the one- and two-stage procedures reported since our paper in 1935. Provided a cholecystogastrostomy and ligation of the common duct is not done, I believe it makes little difference what modification of the one-stage is used.

We regret that our subsequent reports on this subject are seldom referred to and that our original paper describing a two-stage procedure is always mentioned. Because of the newer advances in pre- and postoperative treatment, I condemn the two-stage procedure and advocate the one-stage procedure with choledochojejunostomy and implantation of the pancreatic duct into the jejunum as the procedure of choice.

SUPPURATIVE PANCREATITIS WITH ASSOCIATED LIVER ABSCESS*

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IN ACCORD with our own experience,¹ recent trends in the literature have emphasized the decreased mortality of acute pancreatitis when treated by the conservative nonoperative method, reserving operation for the complications of this disease, namely, pseudocyst and abscess. Within the past three years 19 cases of acute pancreatitis have been encountered in the Jefferson Medical College Hospital, 12 of the edematous type and seven of the hemorrhagic type. In the hemorrhagic group, pseudocyst formation occurred in two cases, and pancreatic abscess, also, in two cases. It is the purpose of this communication to present in detail one case from this series, unusual because of suppuration followed by hepatic abscess, to discuss its pathogenesis and evaluate the factors contributing to recovery.

Case Report—A T, female, age 55, was admitted to the Surgical "A" Ward Service of the Jefferson Medical College Hospital, September 30, 1944, with the chief complaint of epigastric and right upper abdominal pain.

The patient had been well until three days prior to admission, at which time she first experienced moderately severe epigastric and right upper abdominal pain. The pain was constant, did not radiate, and was accompanied by nausea and frequent episodes of vomiting of greenish-yellow material. She also had diarrhea, with passage of four loose stools daily for two days. From the onset of the attack she remained confined to bed and had fever.

The past medical history revealed that the patient previously had always enjoyed excellent health. She had been free of indigestion and was able to tolerate all types of food.

Physical Examination—The patient was a moderately obese middle-aged Italian woman who was apprehensive, slightly irrational, and appeared acutely ill. Temperature 103° F, pulse 130, respirations 26, and blood pressure 140/90. She was slightly jaundiced and markedly dehydrated. The heart and lungs were essentially normal. On inspection, the abdomen was slightly distended and abdominal respiratory movement was restricted. In the right upper quadrant there were exquisite tenderness, marked rigidity and rebound tenderness. No mass was noted at this time. Rectal examination, as well as the remainder of the physical examination, were essentially normal.

Laboratory Data—Examination of the blood showed hemoglobin 78 per cent, red cells 4,000,000, white cells 13,600, with polymorphonuclear cells 57 per cent (8 per cent young forms), lymphocytes 39 per cent, monocytes 3 per cent, and basophils 1 per cent. Urinalysis revealed slight albuminuria, but was otherwise negative. Wassermann and Kahn serologic reactions were negative. The blood urea nitrogen was 90 mg, sugar 114 mg, and serum proteins 6.5 Gm. Van den Bergh test showed a positive direct reaction, with serum bilirubin of 2.1 mg. Bromsulfalein liver function study showed 20 per cent dye retention. The prothrombin time was 68 per cent of average normal.

* Presented before the Philadelphia Academy of Surgery, January 8, 1945.

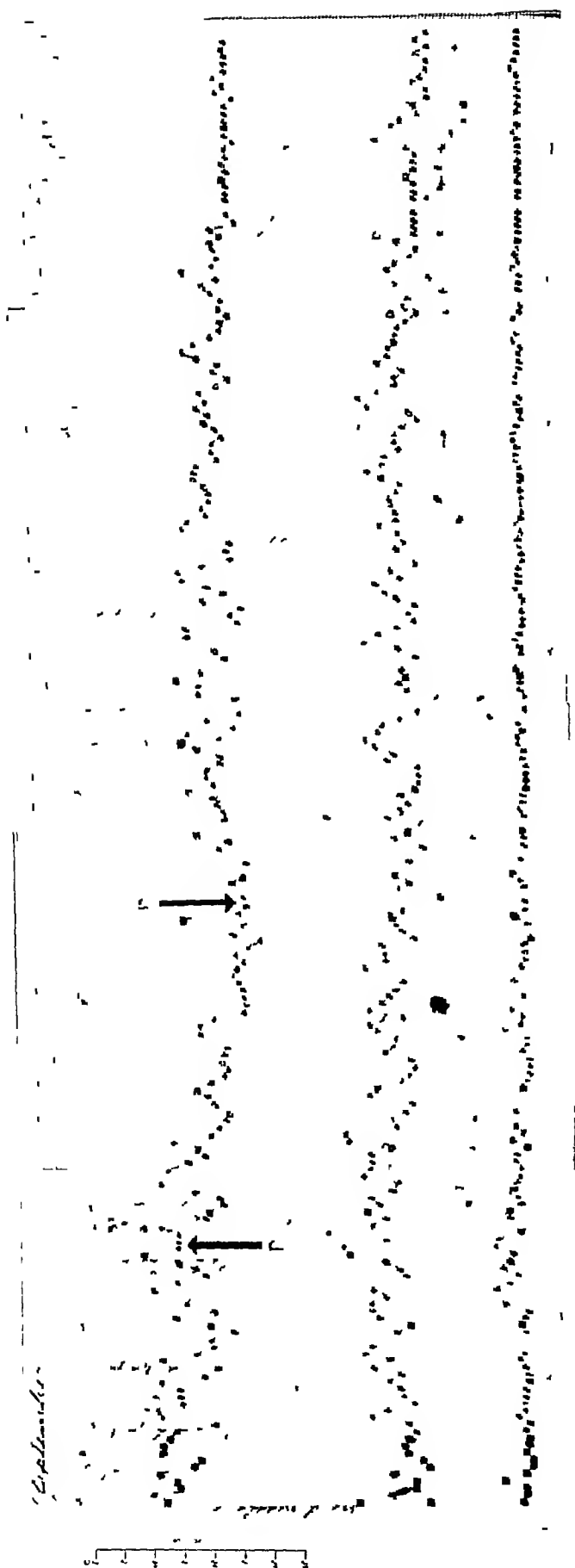


CHART 1 — Vital signs during first hospital admission. Large arrows (P) indicate start and termination of administration of penicillin.

SUPPURATIVE PANCREATITIS

The serum amylase, determined six days following the onset of symptoms, was normal. Blood culture revealed no growth in 48 hours. A plain roentgenogram of the abdomen was negative.

Preoperative Course—It was thought that the patient had acute calculous cholecystitis. Accordingly, a conservative plan of treatment was instituted, consisting of Wangenstein suction, 5 per cent glucose in normal saline solution, with vitamin B₁ 100 mg, vitamin C 100 mg, and vitamin K 4 mg intravenously daily, also sodium sulfadiazine 5 Gm intravenously daily. In spite of this therapy the patient failed to improve, and during the ensuing three days a mass became palpable in the right upper quadrant extending four fingers' breadth below the right costal margin. The temperature fluctuated daily between 100° F and 103° F, and the pulse ranged between 100 and 120. On the fourth day of admission the patient developed grunting, shallow respirations at a rate of between 30 to 40 a minute, but there was no evidence of pneumonitis on physical examination. The leukocyte count rose to 18,000 by the third day of admission, 20,000 by the fourth, and 26,000 by the fifth day. At this time the administration of sodium sulfadiazine was discontinued and penicillin administered intramuscularly at two-hour intervals, with a total dosage of 100,000 Oxford units the first 24 hours and 50,000 units daily thereafter (Chart 1). On the sixth day the patient was operated upon, with a preoperative diagnosis of empyema of the gallbladder, and the contemplated procedure was cholecystostomy.

Operation—Doctor Shallow, October 5, 1944. Under pontocaine spinal anesthesia, a right upper rectus muscle-splitting incision was made, and a slight excess of odorless turbid fluid was encountered in the peritoneal cavity. The gallbladder and biliary tract were free of any inflammatory process, easily compressible, and no stones were palpable. The anterior surface and lesser curvature of the stomach, as well as the duodenum, were next examined and showed no evidence of perforation. The gastrohepatic omentum was markedly congested, edematous, spotted with patchy areas of fat necrosis, and overlay a boggy mass protruding into the lesser peritoneal cavity. The gastrocolic omentum was likewise edematous and involved by scattered patches of fat necrosis. After walling-off the coils of bowel with saline gauze packs the gastrohepatic omentum was incised, and the lesser peritoneal cavity exposed. The posterior wall of the stomach and duodenum showed no evidence of perforation. Within the body of the pancreas was a fluctuant mass, which, following incision, was found to contain about eight ounces of extremely foul-smelling material of thin consistency and dish water color, in which small pieces of necrotic pancreatic tissue were suspended. Subsequent smear of this material revealed necrotic cellular debris, many gram-positive cocci, and the culture was positive for *Streptococcus hemolyticus*. Most of the body of the pancreas was destroyed by the abscess.

The quadrate lobe of the liver, on the inferior surface between the falciform ligament and the gallbladder, presented a slight bulge, suggestive of an underlying abscess. An aspirating needle was introduced and 5 cc of pus was readily obtained. The liver was then incised over this area and a finger introduced. Two abscess cavities, in direct communication, were palpated. Four ounces of foul-smelling, thick, creamy-yellow material were aspirated, which on subsequent smear showed necrotic cellular debris, a few gram-positive cocci, and on culture were positive for *Streptococcus hemolyticus*. This hepatic abscess was entirely independent, showing no continuity or contiguity with the one in the pancreas.

Two iodoform packs and a Penrose drain were inserted into the abscess cavity of each organ and an additional Penrose drain was placed in the kidney pouch adjacent to the foramen of Winslow. These were brought out at the upper pole of the wound, which was then closed in layers. The patient received 500 cc of citrated blood during the operation, which lasted 30 minutes, and she left in fair condition.

Postoperative Course—The immediate postoperative response and convalescence

were essentially uneventful. She received 5 per cent glucose in saline, containing vitamins B, C, and K intravenously daily for four days, Wangenstein suction for four days, sodium sulfadiazine 5 Gm intravenously daily for two days, penicillin 50,000 Oxford units daily in divided doses every two hours intramuscularly for six days (Chart 1), and 500 cc of citrated blood on the seventh and twelfth days postoperatively.

Postoperative Laboratory Data—Blood count (first day) showed hemoglobin 71 per cent, red cells 3,400,000, white cells 19,000 and 5,000 (fifteenth day). Repeated urinalyses were normal. The serum amylase was normal (first day), urea nitrogen 21.4 mg (first day) and 18.8 mg (fourth day), serum calcium 9.2 mg (fourth day), positive direct van den Bergh reaction, with serum bilirubin 1.7 mg (sixth day) and 0.5 mg (21st day), bromsulfalein liver function study showed 5 per cent dye retention (sixth day), and no dye retention (21st day), and blood sugar 99 mg (15th day).

The patient drained purulent material profusely through the wound during the first week, requiring change of dressings several times daily. During this time the jaundice began to subside, the temperature and pulse rate decreased, and the patient's mental state cleared. The drains were started out on the seventh day and completely removed on the tenth. The wound became mildly infected but responded to 0.8 per cent sulfanilamide irrigations and compresses. By the 20th day the jaundice had entirely subsided, the temperature and pulse had become normal and remained so until the patient was discharged, November 4, 1944, the 30th day postoperatively (Chart 1). At this time there was still slight drainage from the wound.

Second Hospital Admission—The patient was readmitted 20 days later, November 24, 1944. Slight drainage from the wound had persisted, and three days before admission she developed fever.

Physical Examination—Temperature 100.4° F, pulse 110, and respirations 20. There was no jaundice, and her general appearance was the same as on discharge from the hospital. An area of tenderness and fluctuation was present in the upper half of the wound.

Laboratory Data—Blood count revealed hemoglobin 65 per cent, red blood cells 3,900,000, and white cells 15,000. Three routine urinalyses were normal. The serum bilirubin was 0.6 mg, bromsulfalein liver function test showed no dye retention, prothrombin time was 52 per cent of normal, and the serum proteins were 5.1 Gm. A plain roentgenogram of the abdomen was essentially negative.

Subsequent Treatment and Progress—The tip of an hemostat was introduced into the upper pole of the wound, and about an ounce of greenish pus, positive on culture for *Streptococcus hemolyticus* and *Staphylococcus aureus*, obtained. The wound was irrigated twice daily, and compressed with 0.8 per cent sulfanilamide solution, and sulfadiazine was given orally so as to maintain a blood level around 5 mg. Vitamin B and K and bile salts were administered orally. Ferrous sulfate was given orally, and 500 cc of citrated blood intravenously, following which the hemoglobin rose to 71 per cent. The patient was discharged, December 9, 1944, 15 days after admission, at which time drainage from the wound was almost negligible.

The patient was last seen January 5, 1945, three months postoperatively. Her appetite was good, she had gained ten pounds in weight, was free of fever, and drainage from the wound had ceased.

COMMENT—Suppurative pancreatitis usually occurs as a complication of hemorrhagic pancreatitis, resulting from bacterial invasion of the necrotic tissue. Less frequently it may occur as a result of ascending infection through the pancreatic duct. Pancreatic abscess has been produced in animals by injection of colon bacilli into the pancreatic duct. Ascending infection may occur when the biliary tract is the seat of inflammation, as in cholelithiasis.

with cholangitis, with reflux of infected bile into the pancreatic duct in the presence of obstruction at the ampulla of Vater (cases of Mayo Robson²) Bevan³ and Batchelor⁴ have each reported a case associated with cholelithiasis. According to Opie,⁵ pancreatic calculi are associated with pancreatic suppuration with relative frequency, and carcinoma compressing the pancreatic duct or carcinoma of the ampulla of Vater (case of Pearce⁶) may, likewise, be

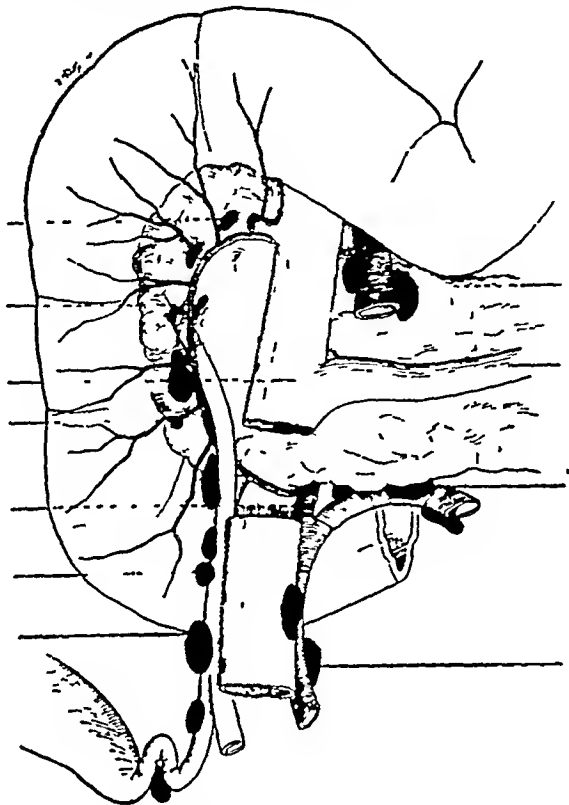


FIG 1.—Posterior surface of duodenum and pancreas, showing relation of lymph nodes along the hepatic artery, cystic and common bile duct chains to those corresponding to the vascular arch behind the pancreas (Poirier, Cuneo, and Delamere)

associated with abscess of this gland. Pancreatic abscess may arise by extension from an adjacent organ by contiguity or through the lymphatics. Thus, abscess in the tail of the pancreas secondary to a perforated gastric malignant tumor has been reported by Ochsner.⁷ Finally, hematogenous spread of infection to the pancreas may occur in rare instances.

Pancreatic abscess is usually associated with peritonitis of the lesser peritoneal cavity, and perforation into the general peritoneal cavity may occur. According to Opie,⁵ rupture into the stomach or intestine has followed, and vomiting or discharge from the bowel of purulent or hemorrhagic material has been reported. Associated thrombophlebitis of the splenic and portal vein may result in metastatic liver abscess. Destruction of a major portion of the gland may lead to the development of diabetes mellitus, as in the case of Beller and Nach.⁸

We believe that the sequence of events in the present case consisted of an attack of acute hemorrhagic pancreatitis followed by bacterial invasion, involvement of the pancreatic veins, and perhaps the splenic vein, by the

infection, and seeding of bacteria or septic emboli into the liver through the portal vein. The spread of infection from pancreas to liver by the lymphatics is also a possibility (Fig 1). The finding of a normal preoperative serum amylase value on the sixth day following onset of the attack is in keeping with the well-substantiated fact, both in the literature and our own cases,¹ that the level usually falls to normal within 12 to 72 hours, and only in the minority of cases is elevated beyond this time (Chart 2).

The absence of biliary tract disease, both in the past history and operative findings, is of interest, since about 70 per cent of cases of acute pancreatitis

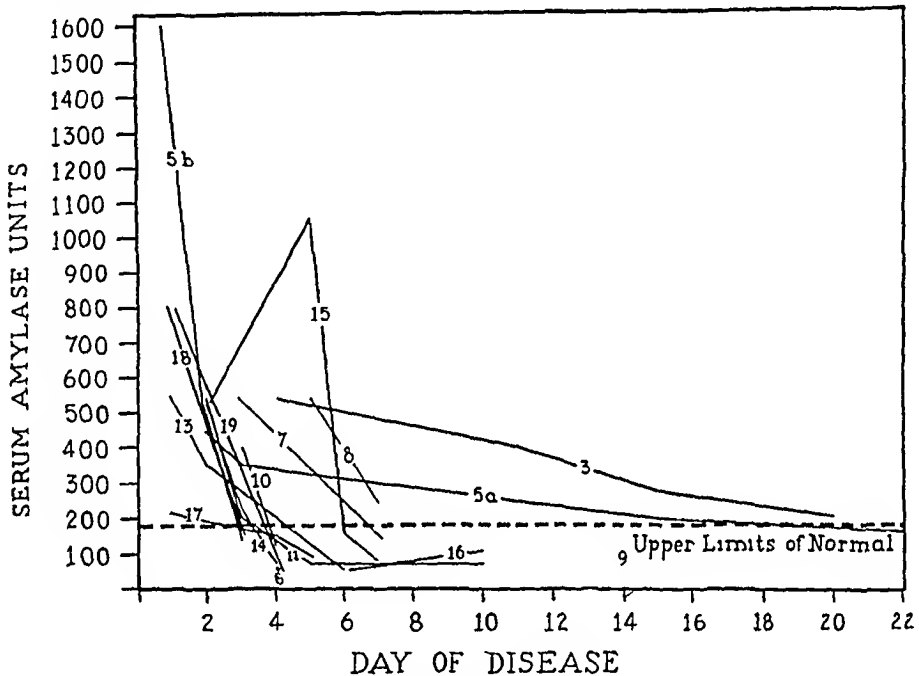


CHART 2—Curves showing elevated serum amylase during acute attack, with fall as attack subsides. (Numbers on curves correspond to cases in authors' series.)

are associated with lesions in this system. The jaundice in this case was mainly due to hepatitis and possibly, to a lesser degree, to compression of the common bile duct in its transit through the gland by edema. Posterior perforation of a peptic ulcer into the pancreas was definitely ruled out at operation. The possibility of an hematogenous origin of the pancreatic abscess seems unlikely in view of the lack of clinical evidence of a primary focus elsewhere, and the negative blood culture.

According to the recent work of Edmondson and Berne,⁹ serum calcium findings below 9 mg per 100 cc of blood usually occur in cases of pancreatic necrosis some time between the second and 15th day of the disease, and values below 7 mg indicate a fatal prognosis. In keeping with this work, the value in the present case of 9.2 mg on the 14th day following onset of the attack seemed to prognosticate a favorable outcome.

In this case the loss of pancreatic tissue did not result in diabetes mellitus. According to the work of Allen,¹⁰ destruction of seven-eighths, or more, of the gland is necessary for a diabetic state to ensue.

The importance of scrupulous pre- and postoperative care in this serious condition is self-evident. Supportive measures, such as fluids intravenously, plasma, blood, and vitamins, Wangensteen suction to combat ileus, and chemotherapy with sulfonamides and penicillin are vital adjuncts in treatment. Because the infection was associated with gram-positive cocci, we believe that the use of penicillin for one week was an important factor in the patient's recovery.

CONCLUSIONS

- 1 Although the conservative nonoperative management of acute pancreatitis has been stressed in the recent literature, this case illustrates a clear-cut indication for surgical intervention, namely, abscess formation.
- 2 The finding of an associated liver abscess at operation is unusual.
- 3 Meticulous pre- and postoperative care, including the use of penicillin, are vital adjuncts to carefully timed and adequate surgical intervention.
- 4 Suppurative pancreatitis with associated liver abscess is a grave but not hopeless condition.

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FROZEN HUMAN SKIN GRAFTS

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PRESERVATION of free skin grafts up to one hour before replacement was begun in 1804 by Baronio¹ Wentscher,² in 1903, was the first to use refrigerated free skin autografts The period of preservation varied from 7 to 14 days Filatov³ treated some skin diseases by transplantation of cadaver skin preserved by refrigeration for several days The transplant itself is lost and the good results are attributed to the production of autocatalyst Refrigerated cornea, mucosa and vascular tissues were similarly employed The same technic was employed with good results by Dellepiane-Rawson⁴

The ability of cold-blooded animals and their organs to survive freezing for periods of time is well known The successful transplantation of various types of tumors after freezing and thawing has been achieved by Klinke,⁵ Breedis⁶ and Cloudman⁷ Mider and Morton's⁸ experiments suggested that skin might survive freezing and thawing in functional conditions

Briggs and Jund⁹ obtained 52 per cent of partial or complete takes using autoplasmic grafts of frozen skin from young mice Slow freezing to minus 78.5° C was employed with slow thawing to 25° or 30° C The period of storage varied from one to 24 hours

Webster,¹⁰ from his extensive experimental work, dating back to 1932, reported a total of 23 patients upon whom refrigerated skin grafts have been applied on 36 occasions Most were split-thickness grafts All but five were autogenous, and in most instances the period of preservation was less than 21 days All autografts refrigerated over three weeks did not take Homogenous grafts, likewise, disappeared Webster also used one graft frozen to minus 72° C and another dried from the frozen state Both were kept for 17 days The frozen graft was largely lost, portions of the skin dried from the frozen state fared better, with about 80 per cent take

In the course of experimental work on the preservation of plasma in the frozen state,¹¹ it was found that under certain experimental conditions it is possible to retain all the physicochemical properties of complex colloids These conditions are essentially rapid freezing, maintenance at a temperature below minus 15° C and rapid thawing followed by warming to 37° C Instantaneous freezing at very low temperatures is neither essential nor does it improve the final product

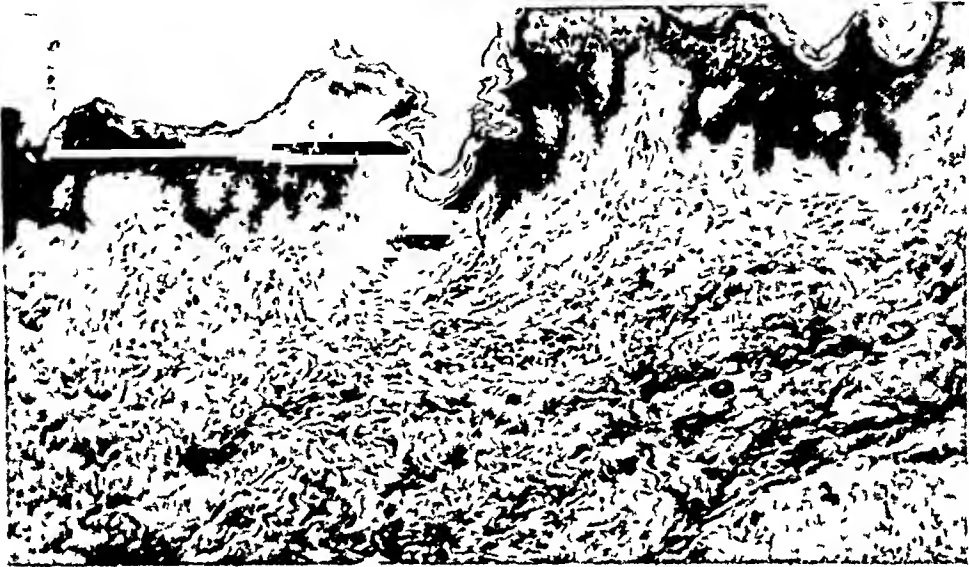
In the process of drying of tissues from the frozen state prior to imbedding in a transparent plastic,¹² it was found that freezing and thawing of tissues from homothermic animals under conditions similar to those just mentioned was compatible with a very good preservation of all cellular structures (Fig 1)

Our experimental work on preservation of human skin in the frozen state was begun in 1943 as a first step in the development of skin banks

FROZEN HUMAN SKIN GRAFTS

for homologous grafts. In the work reported here only autogenous grafts were employed. The technic was as follows. The skin was prepared with green soap, water and ether. Following ether, split-thickness skin grafts were taken from the donor site with the Padgett dermatome¹³. These grafts

A



B

FIG. 1.—A—Normal fresh skin
B—Skin frozen and preserved in the frozen state for three months

measured 0.4 mm in thickness. Segments measuring the full width and length of the Padgett dermatome were obtained and, in turn, these were cut into smaller sections depending upon the size of the recipient area. The controls varied from a section of skin measuring 7.5 cm in width to 20 cm in length to smaller segments depending upon the size and site of the recipient area. The segments of skin to be frozen were of a constant size measuring approximately 10 x 5 x 0.4 mm. These were immediately placed in citrated plasma. The plasma was fresh or preserved in the frozen state. Ten to 15 cc of plasma have been found sufficient for about a dozen pieces of skin. The amount of plasma should be large enough to cover readily all skin pieces.

Pooled plasma as well as plasma from AB-group patients have been used. The best results have been obtained with plasma from AB-type patients. The bottle containing the plasma and skin grafts was closed with a rubber stopper, using aseptic technic and was immediately placed at minus 20° to minus 25° C. With 10 to 15 cc of plasma in an ordinary vaccine bottle complete freezing took place in 15 to 30 minutes, depending on the initial temperature and the method of heat dissipation. The bottles were placed in a slanted position during freezing to minimize danger of breaking.

The skin frozen in plasma was maintained at minus 20° to minus 25° C until ready for use. More rapid freezing or freezing and preservation at lower temperatures have not been found necessary.

At the scheduled time of transplanting, the frozen segments of skin in the plasma were allowed to thaw by placing the bottle in the water bath at 37° C. The skin segments were then transplanted to the recipient site without suturing and using only salt solution to prepare the donor area. A paraffin-mesh dressing over which moist saline sponges were placed followed with a pressure dressing of sponges and Ace bandages were the means utilized to provide uniform pressure. The dressings were not examined until one week had elapsed, and at that time the dressing was changed, and the percentage take was observed. The redressing subsequently was as often as indicated, usually at five-day intervals.

CASE REPORTS

Case 1—A white woman, age 47, was admitted to the Bryn Mawr Hospital January 13, 1944, and discharged on June 8, 1944. The patient suffered from extensive 2nd and 3rd degree burns of arms, forearms, shoulders, thorax, abdomen and back. The 3rd degree burns were most extensive over the right shoulder, the left shoulder, the left forearm and arm and the left thorax, anteriorly and laterally. On February 26, 1944, split-thickness skin grafts were taken from the right thigh and were immediately transplanted as controls to the left arm and forearm. Ten pieces of skin, measuring 10 x 5 x 0.4 mm, were frozen, and next day were thawed and transplanted to the left arm and forearm. On March 5, 1944, all but one of the frozen grafts appeared to have taken. On March 12, 1944, the frozen grafts appeared healthy and showed definite increase in size. On March 7, 1944, split-thickness skin portions were taken from the left thigh and some were immediately transplanted as controls to the left arm and breast. Twelve sections of the size indicated above were frozen. On March 12, 1944, the frozen elements were transplanted to the left arm and breast. On March 19, 1944, there appeared to be six complete takes and two partial takes of the frozen grafts. On March 22, 1944, eight grafts of frozen skin out of 12 appeared viable and proliferating. On March 24, 1944, split-thickness skin grafts were taken from the left thigh. Some were immediately transplanted to the left forearm and 12 segments were frozen. On March 28, 1944, these skin elements were thawed and transplanted to the left forearm. Of the 12 frozen skin grafts, eight appeared to have completely taken, one partially. On April 7, 1944, the takes appeared to be proliferating more than the grafts that were transplanted without freezing.

SUMMARY—The 25 control grafts of fresh skin showed 85.4 per cent takes, the 34 frozen skin grafts showed 78 per cent takes.

Case 2—A white woman, age 78, was admitted to the Bryn Mawr Hospital on April 30, 1944, and discharged on June 17, 1944. The patient suffered from an extensive carcinoma simplex of the left breast with metastasis to axillary lymph nodes. The patient had had a previous right mastectomy in 1940. A radical mastectomy was performed on May 1, 1944. The skin loss was too extensive to perform closure without tension. Moderate sloughing occurred about wound margins, necessitating skin grafting. Split-thickness skin grafts were applied to the left chest, arm and abdomen on June 1, 1944. Three segments of skin, measuring $10 \times 5 \times 0.4$ mm, were frozen. On August 1, after 61 days of preservation at minus 25° C, the three grafts were thawed and

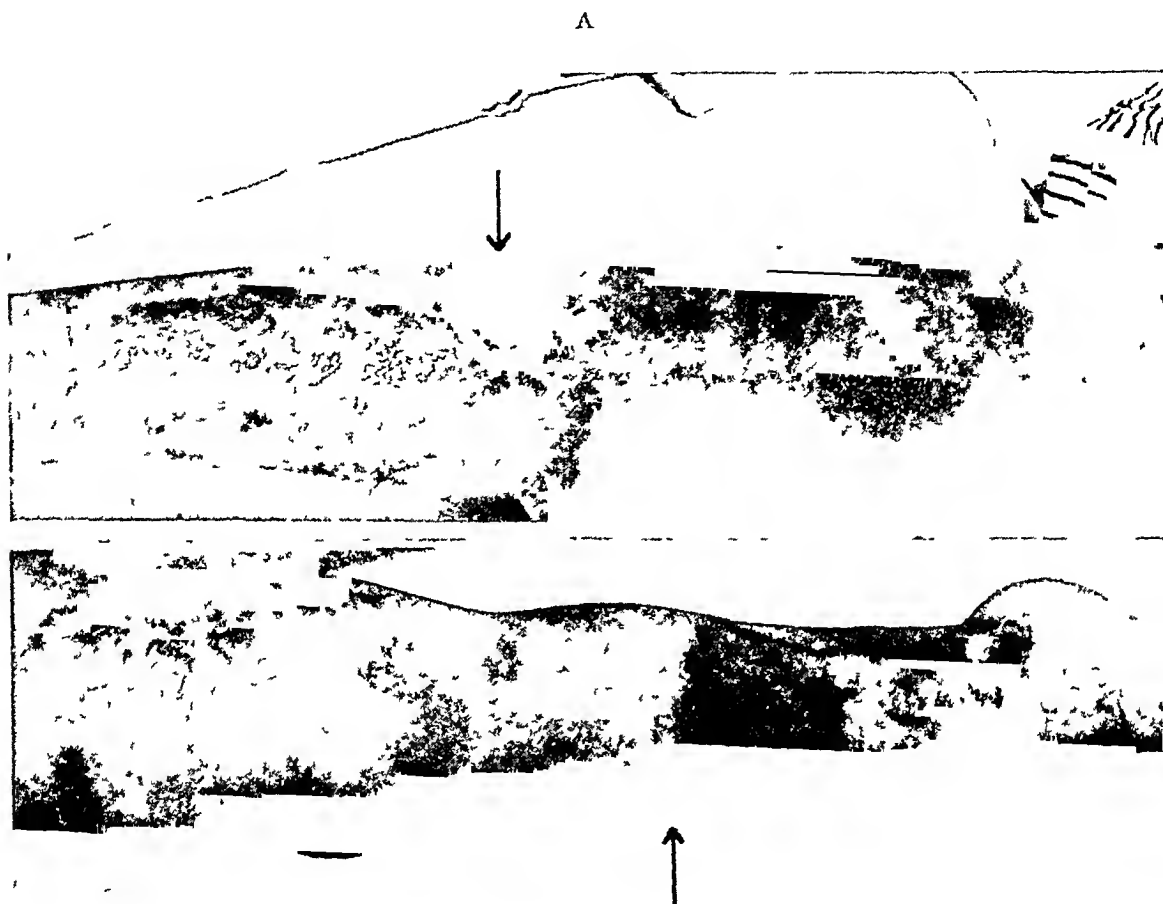


FIG. 2—Case No. 3. Frozen autogenous skin grafts. A—22 days, B—118 days after implantation transplanted to the ulcer on the left thorax. The wound was redressed on August 8, 1944, and all frozen elements appeared to have taken. There was a slight crusting of the frozen elements, with viability appearing certain. By August 15, the grafts appeared to have taken 100 per cent. On September 3, 1944, all refrigerated elements appeared to have taken completely.

SUMMARY—The three control grafts of fresh skin showed 85 per cent takes, the three grafts of frozen skin showed 100 per cent takes.

Case 3—A white male, age 5, was admitted to the Bryn Mawr Hospital on March 16, 1944, and discharged on June 4, 1944. He suffered from extensive 2nd and 3rd degree burns of the arms, forearms, thighs, leg and face. Split-thickness skin grafts were removed on May 4, 1944. Some were immediately transplanted to the left leg and thigh. Four pieces, measuring $10 \times 5 \times 0.4$ mm, were frozen. On May 11, seven days later, the frozen skin grafts were thawed and implanted on the left leg. On May

17, the grafts appeared to have taken nicely. On June 24, 44 days after implantation, all grafts were doing well. Those which had been frozen appeared to be somewhat healthier than the control grafts at similar stages and were proliferating more than usual (Fig 2). On September 11, four months later, all grafts had continued to grow nicely and had formed viable skin.

SUMMARY—The six control grafts of fresh skin showed 96 per cent takes, the four grafts of frozen skin showed 100 per cent takes.

SUMMARY AND CONCLUSIONS

Forty-one autogenous split-thickness grafts preserved in the frozen state from one to 61 days at temperatures of minus 20° to minus 25° C were transplanted to three patients. These grafts resulted in 80.5 per cent permanent takes. Thirty-four control grafts of fresh skin in the same patients resulted in 86.4 per cent takes.

The result of grafting does not appear to be affected by the time of storage of the grafts in the frozen state, at least within the experimental limits mentioned.

Aside from the possible development of skin banks for homografts, the preservation of split-thickness autogenous skin grafts in the frozen state allows the operator to obtain at one operation large numbers of grafts which may be employed for transplantation at any time later on.

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THE PYRUVIC ACID METHOD OF BURN SLOUGH REMOVAL

AN EXPERIMENTAL INVESTIGATION*

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THERE IS GENERAL AGREEMENT that the process of repair in any type of wound is favored by the early and complete removal of nonviable tissue. In the contused laceration, this débridement is accomplished by excision with



FIG. 1.—Condition of three experimental burns on Dog No. 7, on fourth day. Left upper, plain starch paste. Right upper, pyruvic acid paste. Small, irregular sloughs have been removed as indicated. The wounds are identical. Finger points to dry control, with no sign of sloughing.

the knife. Although such straightforward surgical treatment has been applied to burns occasionally, it has been assumed that a chemical method of slough removal would be preferable, owing to the difficulty in making an early and accurate determination of which areas will ultimately prove to be third-degree in depth.

Connor and Harvey¹ have described a procedure for the treatment of

* This work was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Development and the Henry Ford Hospital.

PYRUVIC ACID IN BURNS



FIG 2—Dog No 8 on fourth day. The sloughs are more clean cut in this instance. No difference in effect of pyruvic acid paste and plain paste.



FIG 3—Dog No 11 on the fourth day. Note the vascularized appearance of the granulating bases.

experimental third-degree burns which results in a surprisingly early separation of the slough. They reported a pleasing result in one clinical case. They had recalled that infection is often associated with rapid slough separation and had noted that the p_H of the exudate from the infected wound was frequently low, i.e., of acid reaction. Therefore, the basis of their method was to bring the wound into an acid environment as far as possible. This



FIG 4—Effect of plain starch paste (left anterior burn) and tragacanth jelly (right anterior burn). Good sloughing of both occurred on fourth day.

was done by dressing the lesion with a generous amount of a paste containing enough pyruvic acid to bring the p_H down to 1.9. Small third-degree burns in dogs were produced by burning for 20 seconds with a gas flame. "The control burns were dressed within a few hours after burning with either dry gauze, vaselined gauze or a paste consisting of 8 per cent cornstarch in distilled water." The control wounds sloughed in 10 to 12 days. The burns treated with pyruvic acid paste sloughed in three days.

We have repeated this experiment with two changes in the procedure. A method of burning was used which probably produced a more uniform burn, and every treated lesion was checked with *two* controls on the same animal, one was left dry and the other was covered with the vehicle for the pyruvic acid, i.e., plain starch paste.

Small or medium-sized dogs were used. A suitable area on the back was shaved, after which the animal was anesthetized with intravenous

PYRUVIC ACID IN BURNS

nembutal For making the burn, we used the flattened bottom of a pyrex test tube containing sulphuric acid which had been heated to 205° C At the instant of contact, the temperature was usually about 200° C and

TABLE I

Dog No.	Seconds of Burning	Days Required for Sloughing		
		Plain Starch	Pyruvic Acid	Dry Control
1	15	3	3	17
2	45	4	4	9
3	15	4	4	11
4*	15			
5	15	4	5	11
6	30	4	4	11
7	30	4	4	13
8	30	4	4	11
9	30	1	4	9
10	30	5	5	10
11	30	4	4	11
12	30	4	4	11

*None of the burns on this animal sloughed, due to short period of burning

at the end of 30 seconds of burning was about 190° C Two burns were placed anteriorly, one on each side The third burn was placed posteriorly near the midline In the first series of 12 animals, the right anterior burn was covered with the pyruvic acid paste, the left anterior was

TABLE II

TRAGACANTH JELLY *versus* PLAIN STARCH PASTE

All Burns were for 30 Seconds

Dog No	Days Required for Sloughing		
	Plain Starch	Tragacanth Jelly	Dry Control
B1	4	4	12
B2	3	3	11
B3	3	3	10
B4	3	3	10
B5		4	9
B6		4	7*

*Animal licked dry control wound
(Only two burns made on animals B5 and B6)

covered with the plain paste, and the posterior burn was left dry and exposed To prevent mixing of the two pastes, a "bridge" of dressing was placed between the wounds Both layers of paste were covered with vaselined gauze and dry gauze, after which a substantial circular bandage of elastoplast was applied During the first few days, additional paste of the appropriate kind was forced under the dressing by means of a small syringe of the asepto type At these times, it was possible to get a partial view of the wound to see if sloughing was about to take place

Figure 1 is typical of the appearance of the wounds on about the fourth day The areas treated with either the pyruvic acid paste or the plain starch usually sloughed in the same period of time (3-5 days) while the dry

control needed about 12 days. Sometimes the sloughs were ragged, as in Figure 1, at other times they were clean-cut buttons (Fig 2) and occasionally they were lost entirely (Fig 3). The base of subcutaneous tissue which remained after the removal of the slough appeared to be healthy, as if it would take a skin graft.



FIG 5—Dog No 21 on the second dry. Upper wound dressed with wet cotton has sloughed. Dry control wound shows no sign of sloughing.

This experiment was carried out in 12 animals (36 burns), and the results may be seen in Table I. In no instance did the pyruvic acid paste prove to be superior to the plain starch paste.

We then repeated the experiment, substituting a presumably inert aqueous jelly base (tragacanth) for the pyruvic acid paste. The results in six animals are shown in Table II. The tragacanth jelly proved to be as efficacious in removing slough as either of the agents used in the preceding experiment (Fig 4).

From the above experiments it appeared likely that sloughing would be promoted by keeping the burn *moist* by any method. Therefore, in the third set of experiments, only two burns were made on each animal, an anterior one which was dressed with absorbent cotton wet with distilled water, and a posterior dry control (Fig 5). Table III gives the results obtained in nine dogs.

PYRUVIC ACID IN BURNS

COMMENT

Early sloughing was produced by dressing the small third-degree burns with pyruvic acid in starch paste, plain 8 per cent starch paste, tragacanth

TABLE III

Dog No	Days Required for Sloughing	
	Wet Cotton	Dry Control
13	4	9
14	6	22
15	4	15
16	5	16
17	Died (anesthesia)	
18	15*	16
19	3	14
20	3	11
21	2	9

*Vicious animal Dressing received only initial wetting, and became dry

jelly and cotton wet with distilled water The only common factor appears to be the "wetness" It is suggested that the favorable effect on sloughing obtained with pyruvic acid paste is due more to maceration than to p_H A dry gangrene has been converted to a wet one

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BONE SARCOMA IN POLYOSTOTIC FIBROUS DYSPLASIA*

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WITHIN THE PAST DECADE the syndrome now commonly designated as fibrous dysplasia of bone has become increasingly recognized. In 1934, Goldhamer¹ recognized a disease which he characterized as osteodystrophia fibrosa unilateralis with pubertas praecox, and, in the same year, Borak and Doll² described what they called unilateral Recklinghausen's disease of bone with pubertas praecox. Almost simultaneously in this country appeared papers by Lichtenstein, who employed the term "polyostotic fibrous dysplasia," and by Albright, Butler, Hampton and Smith⁴ and Albright, Scoville and Sulkowitch,⁵ who defined the process as a syndrome characterized by osteitis fibrosa disseminata, areas of pigmentation, and endocrine dysfunction, with precocious puberty in females. In 1942, Lichtenstein and Jaffe,⁶ published an account of a large number of cases, with descriptions of their accessory features in addition to the skeletal lesions.

The present authors have no intention of again describing the syndrome. Their sole purpose is to place on record two instances of malignant bone tumor arising on the basis of fibrous dysplasia. Heretofore, so far as they know, this event has not been described, although cases doubtless exist.

In our first case, initially seen in 1929, the syndrome was, quite naturally, not recognized, although the characteristic pigmentation is described. Not until about ten years later did this case reach the proper clinicopathologic category.

CASE REPORTS

Case 1.—The patient, J W, No 40833, was a female, age 42, of Lithuanian ancestry. Her past history was uneventful. Five months prior to admission, she noted slight stiffness in her left shoulder. This increased during the following month and pain developed, especially on motion. Apparently, she first noted swelling in the shoulder region about two months after her first symptom. The swelling became progressively worse and two weeks prior to admission to the Memorial Hospital, the patient entered another hospital where a presumptive diagnosis of malignant bone tumor was made, whereupon she was referred to Memorial. During the two months prior to admission, the patient had lost about eight pounds in weight, suffered from occasional headaches and complained of a burning sensation over the left anterior chest wall.

The pertinent part of the initial examination concerns the local condition and the radiographic findings. The left scapula was the site of a large tumor mass, firm, rounded, nontender, possibly somewhat fluctuant. The entire shoulder region, anterior and posterior chest walls were the site of a brownish pigmentation which extended upward both anteriorly and posteriorly in the neck region. This pigmentation was essentially unilateral but reached slightly beyond the midline (Figs 1 and 2).[†] There was marked limitation of motion of the left arm, abduction was essentially absent and anteroposterior motions were but moderate.

* Submitted for publication February 17, 1945.

† 1941 photos, roentgen changes present in pigmented areas.

FIBROUS DYSPLASIA AND SARCOMA



FIG 2—Pigmentation and enlargement of scapular area due to tumor. A late photograph.



FIG 1—Typical pigmentation essentially unilateral in character. Late photograph after treatment by irradiation. In the shoulder area the pigmentation changes are partly the result of irradiation.

Films of the left shoulder taken November 21, 1929, (Fig 3) showed almost complete loss of outline of the left scapula which was replaced by a very large tumor mass, completely osteolytic, with only a few bony remnants remaining. The entire shaft of the left humerus showed altered architecture, with thinned cortex and multiloculated appearance of the medullary cavity.

Films of the chest of the same date (Fig 4) showed marked deformity of most of the ribs, particularly on the left, with irregular expanded multiloculated areas. The lung fields appeared clear.



FIG 3—Osteolytic lesion of left scapula. Humeral architecture with thinned cortex and multiloculated medullary cavity.

Films of the spine, pelvis and femora (Fig 5) taken in December, 1929, showed no changes in the spine but the left ilium and the right pubis showed slight expansion and areas of decreased density similar to those seen elsewhere. Both femora showed widespread changes with decrease in density of the medullary cavities which latter were irregularly expanded.

Lateral films of the skull (Fig 6) showed a pagetoid appearance of the entire skull and facial bones, with thickening of the tables and irregular areas of decreased density.

The scanty laboratory studies during this patient's first admission revealed nothing of significance unless a basal metabolic rate of plus 20 is indicative of some hyperthyroidism, since the latter has been emphasized in this disease. An aspiration biopsy was performed and yielded rare large atypical spindle cells, diagnostic of some type of sarcoma. Hence, a tentative diagnosis of medullary spindle cell sarcoma of bone was made.

The tumor was not considered suitable for radical surgery, since at that time it was not realized that the process in other areas was probably not sarcomatous, and the patient received a rather small amount of treatment with a radium emanation pack. This totaled but 28,000 mg hrs at 6 cm, and was administered on five successive days, between November 19, 1929, and November 23, 1929, through anterior and posterior portals. At the same time the patient received three roentgen-ray treatments to the left shoulder region, two over the rib areas and two to the skull, and between November 27, 1929, and January 7, 1930, she received Coley's toxin both intramuscularly and intravenously, with, on the whole, rather little reaction. Despite the seeming total inadequacy of the radiation, the patient's condition considerably improved. The tumor diminished in size, pain became much less severe and eventually vanished except for what the patient described as "slight pain with weather changes."

Radiographic reexamination of the left shoulder on December 24, 1929, showed a marked improvement in the appearance of the scapula, with marked decrease in size of the tumor and beginning calcification suggesting regeneration.

The patient was again able to conduct her housework in a normal fashion and persistently refused to return to the clinic for observation. In fact, despite numerous appeals, she remained away for 11 years.

She reentered the Hospital on July 9, 1941, and so far as the local findings were concerned the situation in the left shoulder was somewhat improved over that observed in 1929. Radiographs were reported as follows:

"Reexamination of the left shoulder on July 10, 1941, shows some residual soft-part tumor, but there has been marked regeneration of the scapula, with reformation of the glenoid and vertebral border. The humerus shows no significant change from previous status."

Films of the chest on July 10, 1941, showed no apparent new changes in the ribs but there was increased density over the left chest, probably due to radiation. There was a large rounded shadow in the periphery of the right upper lung field which had the appearance of metastasis. The right humerus appeared normal. The pelvis showed no significant change. The skull again showed extensive changes which were better demonstrated and seen to be largely on the left.

The pigmentation was unchanged except for the addition of a large area of roentgen pigmentation, with scaling and telangiectasia. The patient's general condition had considerably declined. On this admission the laboratory studies were considerably more extensive. Red blood cells ranged from 25 to 29 million, except for a transient peak following transfusion. Calcium varied from 10.0 to 13 mg, phosphorus from 2.82 to 4.11 mg, alkaline phosphatase from 178 to 280 mg, acid phosphatase was 0.56



FIG 4—Rib deformity with numerous expanded multiloculated areas

units Serum protein level on two determinations showed 78 and 81 per cent Prothrombin level was 51 per cent Chlorides ranged from 582 to 591 mg Chloride tolerance was abnormal and appeared suggestive of adrenal cortical insufficiency Blood cholesterol studies showed total cholesterol 1643 mg, free 557 mg, esters 1086 mg Bence-Jones studies were negative on several occasions Two basal metabolic rate determinations were reported as plus 25 and plus 20



FIG 5—Expanding areas of decreased density in femur

Shortly after admission, but after a second aspiration biopsy, the patient developed a septic temperature ranging up to 103° F, and since no cause could be otherwise elicited, it was assumed that the source was infected tumor tissue On July 30, 1941, an open biopsy was made of the scapular tumor

The tumor tissue was soft, friable, yellowish to grayish, in places very hemorrhagic It was about the consistency of chicken fat clot On section (Fig 7), it proved to be a highly pleomorphic, nonbone-forming, spindle and giant cell sarcoma Giant cells reached enormous proportions and numerous atypical mitoses could be found It was quite obvious that the tumor cells were identical with those obtained in the first material aspirated in 1929, and in the subsequent aspiration This should be sufficient to dispel any doubt as to the existence of a malignant process in 1929, even in the mind of sceptics of aspiration as a diagnostic method, but poses a difficult question as to why a large osteolytic malignant tumor had remained for so many years prior to dissemination This naturally is a question which the authors are unable to answer

Since it became desirable to prove, by something other than radiographs, that this lesion had arisen on a basis of polyostotic fibrous dysplasia, it was determined to biopsy a supposedly nonneoplastic area for confirmation of this diagnosis. Hence, on August 14, 1941, an 8.5-cm portion of left 8th rib was removed. On section, this tissue showed no evidence of tumor, and fulfilled all criteria for a microscopic diagnosis of fibrous dysplasia.



FIG 6—Pagetoid areas in skull and facial bones. An anteroposterior view revealed these to be mainly unilateral.

The patient was discharged, August 28, 1941, clinically improved. Again, she failed appointments, but this time evidently because of progress of tumor. Repeated attempts to persuade her to return to the hospital failed and she died at home on December 2, 1941. During the terminal phase of the illness she complained of abdominal discomfort, diarrhea and, evidently, the tumor of the left scapula had ulcerated and begun to fungate. A letter from her family physician stated that she had developed "intestinal" metastasis. Naturally, the authors are unable to confirm this finding in the absence of autopsy but in view of the radiographic finding in the right chest, see no reason to doubt the presence of abdominal disease.

Obviously, this tumor ran a most unusual clinical course. It was diagnosed as malignant bone tumor in 1929 on pathologic evidence, which we believe entirely reliable. With treatment, which should not have sufficed to control it, the patient experienced prolonged relief of symptoms, with regression and apparent quiescence of the tumor, and remained in relatively good condition for over 11 years.

Case 2—The second patient, G deP, No 55274, was a male Italian, age 34. His past history was uneventful except for a primary luetic lesion many years prior to admission for which limited treatment had been given. His present illness began nine months prior to admission, when he noted pain in the left lower thigh and leg. This became worse and, about three months prior to admission, swelling of the left hip was first noted. The swelling increased rapidly in size and was accompanied by severe pain.

On admission, there was a bulky tumor mass involving the left hip laterally and posteriorly, and measuring 24 x 20 cm in greatest dimensions. There was marked tenderness laterally over the greater trochanter. The bulk of the tumor was situated

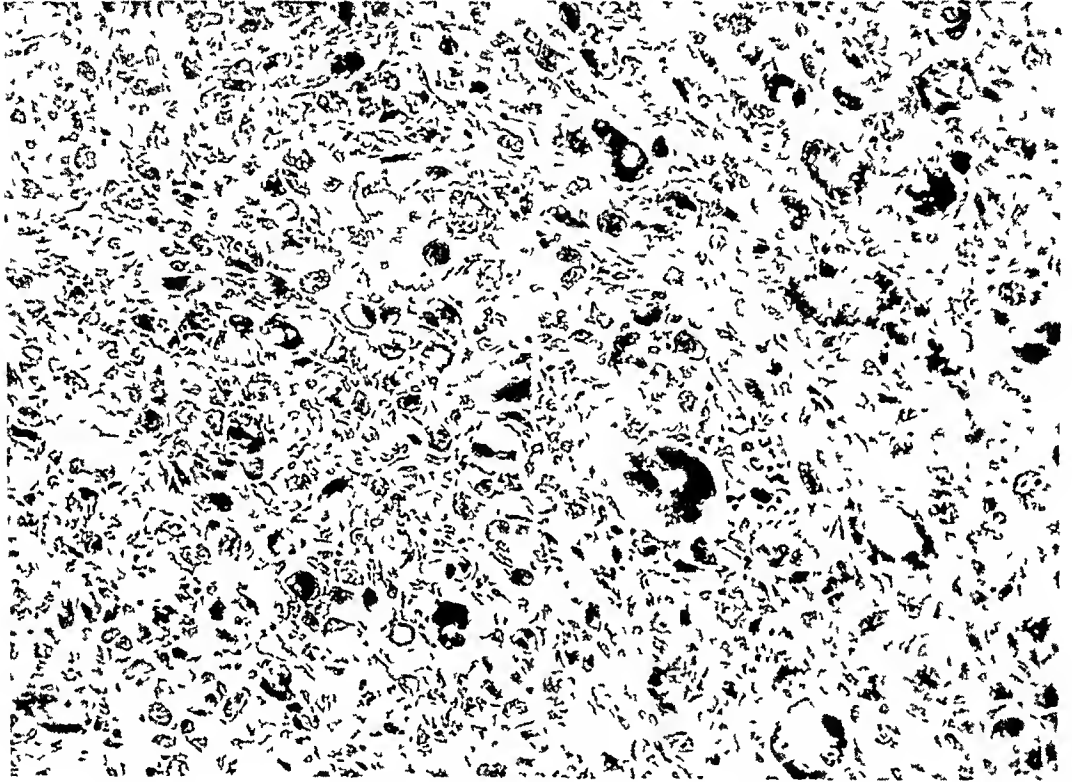


FIG 7—Pleomorphic large spindle and giant cell sarcoma

posteriorly and was of firm, rubbery consistency. There was limitation of motion of the left hip in all directions mainly because of pain. There was no increase of local heat.

Films taken at the time of admission revealed a pattern considered classical for fibrous dysplasia. There were multiple somewhat expanding areas of bone rarefaction, together with zones of increased density involving the left pubic bone, left femur particularly the neck region, and left tibia (Figs 8 and 9).

On May 25, 1938, an aspiration biopsy was performed and a few cells were recovered which suggested malignant tumor. On May 31, 1938, the aspiration was repeated and a giant and spindle cell sarcoma, consistent with primary spindle cell sarcoma of bone, was diagnosed, both on smear and sectioned fragments of clot (Fig 10). The resemblance to the previous case was striking.

Blood calcium ranged from 10 to 10.8 mg, blood phosphorus from 2.6 to 3.8 mg. Phosphatase which ranged from 10 mg on admission to 24.9 mg on June 17, 1938, fell with treatment to 5.7 mg on August 17, 1938. His basal metabolic rate was reported as plus 35, but for certain reasons this was considered inaccurate.

The patient was treated by roentgen ray, receiving a total of 18 treatments between

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June 1, 1938, and June 21, 1938 Portals were anterior, lateral and posterior, approximately 15 x 18 cm each Daily doses were 300 r for a total of 1800 r per port The patient experienced remarkable relief from pain, this relief being much more than would be expected for the ordinary malignant bone tumor Flexion and extension returned to a considerable extent On January 4, 1939, radiograms of the femur revealed considerable evidence of bone regeneration



FIG 8

FIG 9

FIG 8—Multiple expanding areas of decreased density together with zones of increased density, left pubis and femur

FIG 9—Similar areas of decreased and increased bone density, left tibia

On March 8, 1939, the clinical improvement was regarded as so paradoxical that the question was raised as to the correctness of the diagnosis of osteogenic sarcoma On November 8, 1939, the patient reported that he was essentially free from symptoms and no tumor was palpable, although diffuse thickening and firmness of muscles and subcutaneous tissues were noted When referred for a check-up radiographic examination of the pelvis and left femur, however, he was found to have a pathologic fracture in the region of the intertrochanteric line with considerable shortening of the femoral shaft and coxa vara deformity Approximately two months later further examinations showed no significant change It appeared that a diagnosis of spindle cell sarcoma in an area of fibrous dysplasia was warranted, but to make more certain it was decided to obtain

tissue from the involved area of tibia and an open biopsy was performed on February 8, 1940. This tissue was reported as fibrous dysplasia.

The patient returned to the Follow-up Clinic until July 15, 1942. He had remained essentially symptom-free. In August, 1942, he entered another hospital complaining of epigastric pain and vomiting. His condition grew progressively worse and death occurred eight days after admission. No autopsy was obtained. Radiographs, however, are described as revealing an enlarged hilar shadow, with pulmonic infiltration, retraction

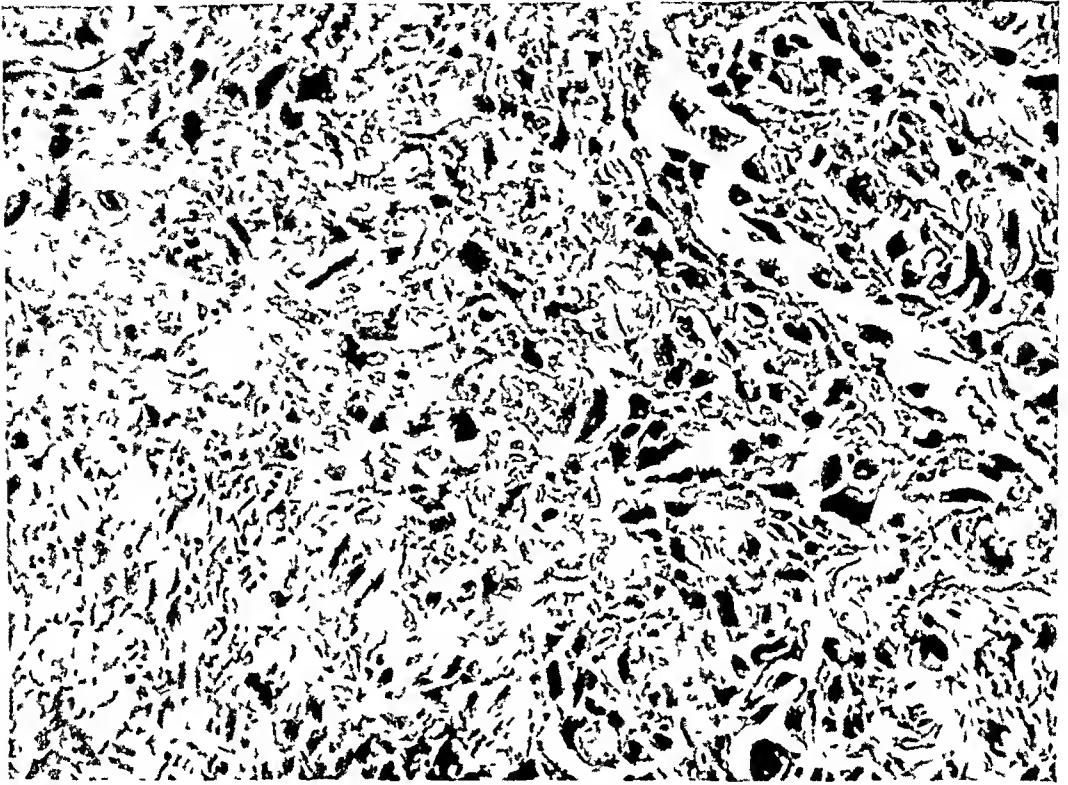


FIG. 10—Pleomorphic spindle and giant cell sarcoma of left femur

of heart and trachea to the right, thickened pleura, partial atelectasis of right lung. The radiologist's conclusion was tumor of the left hilar region with metastasis to bone. Naturally, the evidence points entirely toward the left femur as a primary source of tumor. Again, in the absence of autopsy, one cannot be absolutely certain that metastasis had occurred, but given the radiographic evidence pointing to metastasis, with full knowledge that a malignant bone tumor existed, a doubt seems scarcely justified.

SUMMARY

In conclusion, it may be stated that (1) polyostotic fibrous dysplasia may be added to the group of diseases of bone which may, in certain instances, develop malignant bone tumors. (2) In the two examples so far studied by us, the tumors have been essentially identical histologic pattern, namely, non-bone-forming pleomorphic spindle and giant cell sarcomas. (3) Both tumors appear to have produced metastases. (4) In both instances the response to radiotherapy has been unusual when compared to expected behavior of similar histologic types in different clinical settings. Whether this behavior will eventually prove part of a general clinical entity or not must await further cases.

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FINNEY-HOWELL FOUNDATION FELLOWSHIPS

At the meeting of the Board of the Finney-Howell Research Foundation, Inc, on March 2, 1945, fellowships were renewed for the third year for Dr Nelicia Maier, for the second year for Drs Muriel Virginia Bradley and Margaret Aston Kelsall, and a new fellowship was awarded Dr Elizabeth Cavert Miller, to work in the University of Wisconsin

Applications for fellowships for 1946 must be made to this office before December, 1945, to be eligible for consideration

SPONTANEOUS RUPTURE OF AXILLARY ARTERY

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THE CASE to be reported is one of spontaneous rupture of the right axillary artery in a boy of fifteen. This followed a slight muscular effort, and ended in fatal hemorrhage. The autopsy disclosed unusual and unfamiliar alterations of the arterial wall, not only in the ruptured vessel but in several other intact medium-sized arteries. The extreme rarity of such an accident—only one similar case having come to our notice in a review of the literature—justifies a brief report.

Case Report—Unit No 727939. I D, a 15-year-old French school boy, was admitted to the Presbyterian Hospital complaining of pain, swelling, and discoloration of the skin and soft tissues about the right shoulder. Four days before admission, while playing football and throwing a "forward pass," he experienced a sudden sharp pain beneath the right clavicle with concurrent tingling sensation in the right arm, forearm, and hand. He stopped playing, and was without symptoms for 24 hours, except for soreness in the right pectoral region. Thirty-six hours after the original pain, while straining at stool, he felt a sudden swelling beneath the right clavicle and reported to the school physician who found the radial pulse normal, with no difference between the two sides, R B C 4,220,000, W B C 11,000, coagulation time 2.25 minutes, and bleeding time 2.75 minutes. The swelling progressed, occupying the entire upper pectoral region, and on the fourth day, the right radial pulse could no longer be palpated. The boy became pale and fainted several times during the day, his blood pressure fluctuated between 104/70 and 125/50. Color and temperature of the right arm were always good, but because of symptoms he was brought to the hospital.

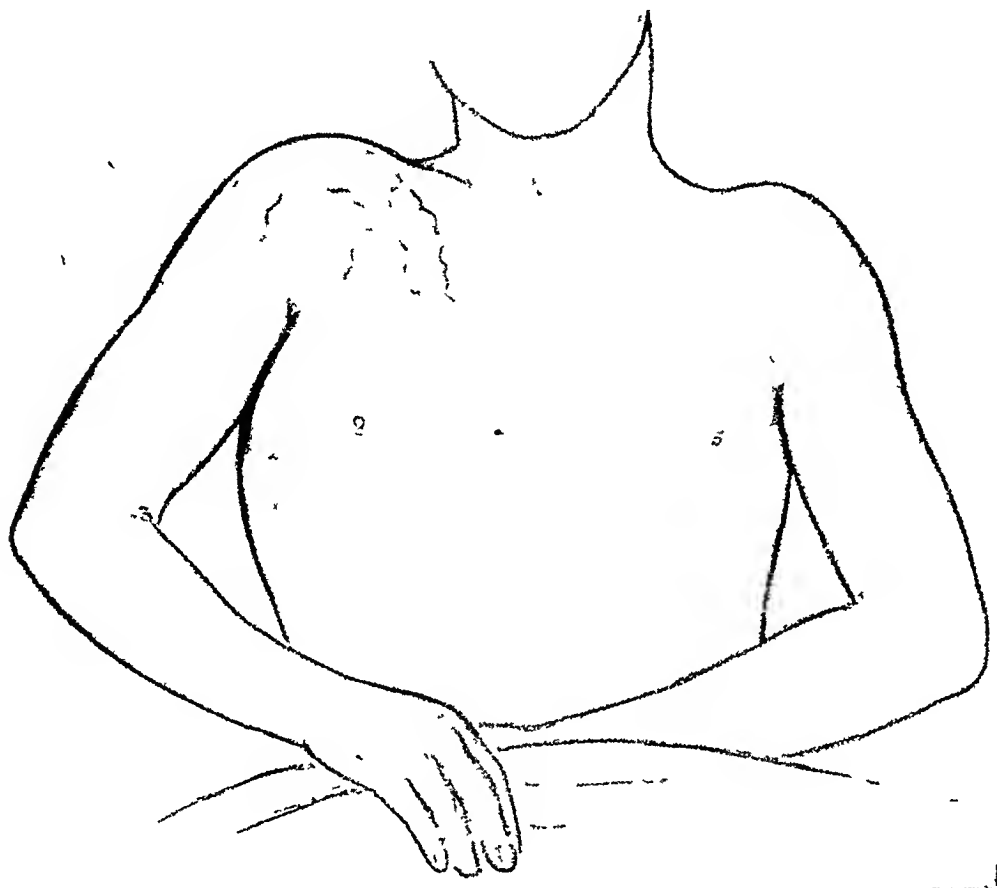
The family history was irrelevant, but in the past history there are several pertinent facts. The boy was born in France and lived there until 1941. He was a six weeks premature baby weighing 3.5 pounds. As a child he was delicate and showed bruises from the slightest trauma. He had noticed, also, that any abrasion or cut bled longer than usual. Despite this hemorrhagic tendency, he had always been active in sports and athletics. No history of chronic or infectious diseases except diphtheria at the age of twelve for which he received diphtheria antitoxin. One year prior to admission, he had been hit in the right upper chest, just below the right clavicle, with a soft baseball. Soreness and slight swelling developed in this region following the trauma, but subsided in a few days without any other symptoms or untoward effects.

Physical Examination—At time of admission. Temperature 99.8° F, pulse (left radial) 124, (right radial) 0, respirations 22. The patient was a well-developed asthenic youth, pale, uncomfortable, and apprehensive. There was a swelling in the right pectoral region extending from the clavicle downward under the pectoral muscles and laterally into the axilla. Areas of ecchymosis were present over the axillary portion of the swelling, and the superficial veins over the right supraclavicular region were dilated and prominent. The right upper arm was slightly swollen (drawing). Both arms were equal in color and temperature, but no right radial pulse or blood pressure could be obtained. The remainder of the physical examination was irrelevant.

Laboratory Data—Blood group O, Rh positive. Hb 47 per cent, R B C 2,530,000,

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WBC 24,500, 62 per cent neut, 35 per cent lymph, 3 per cent mono, hematocrit 21.4 per cent, platelets adequate, prothrombin time 11.9 seconds, plasma proteins 5.54 Gm per cent, venous clotting time 4.25 minutes. Roentgenogram of the chest. Lung fields clear. There is a line of increased density on the inner margin of the right apex. The soft tissues of the right lateral chest wall and axilla are markedly widened so that they measure about 10 cm as compared to 3 cm on the left side. This undoubtedly represents a large soft-tissue swelling, which probably overlies the chest and accounts for the increase in density in the right chest. Urine. Before operation 1+ albumin and an



Drawing showing appearance of the patient at time of admission

occasional granular cast in the sediment, sp gr 1.027, the day following operation, the urine was normal, with sp gr of 1.017.

Course in Hospital—First hospital day. After securing blood for grouping and cross-matching, the patient was taken to the operating room. The operation, however, was postponed as it was deemed expedient to improve his condition by transfusions of blood and plasma and infusions of saline because of his shock-like state and because of the extreme blood dilution caused by the hemorrhage. He was transfused with fresh citrated blood, 500 cc, from a professional donor. This was followed by 500 cc of normal saline.

Second hospital day. The increased pain, axillary swelling, further decrease in both the hematocrit and plasma proteins indicated further internal hemorrhage demanding operative intervention. To prepare him for surgery, 500 cc of fresh citrated blood from a professional donor and 1,000 cc of recalcified plasma were transfused.

Operation—Exploration and ligation of axillary artery and vein, partial expression of hematoma.

Pathology "The pathology was one of the most striking pictures which we have seen of extravasation of an enormous amount of blood in the subpectoral region, outlined mesially and caudad by the limitations of the pectoral fascia and origin of the muscle. The skin of the chest wall was pushed forward for distance of 10+ cm by an enormous hematoma beneath the pectoralis major primarily, extending from the midline to the lower ribs and laterally in the subscapular region and, in addition, pushing the shoulder cephalad to a marked degree. The axillary artery was torn through completely, presenting an irregular margin of all its coats. It seemed softer than normal. The axillary vein was intact."

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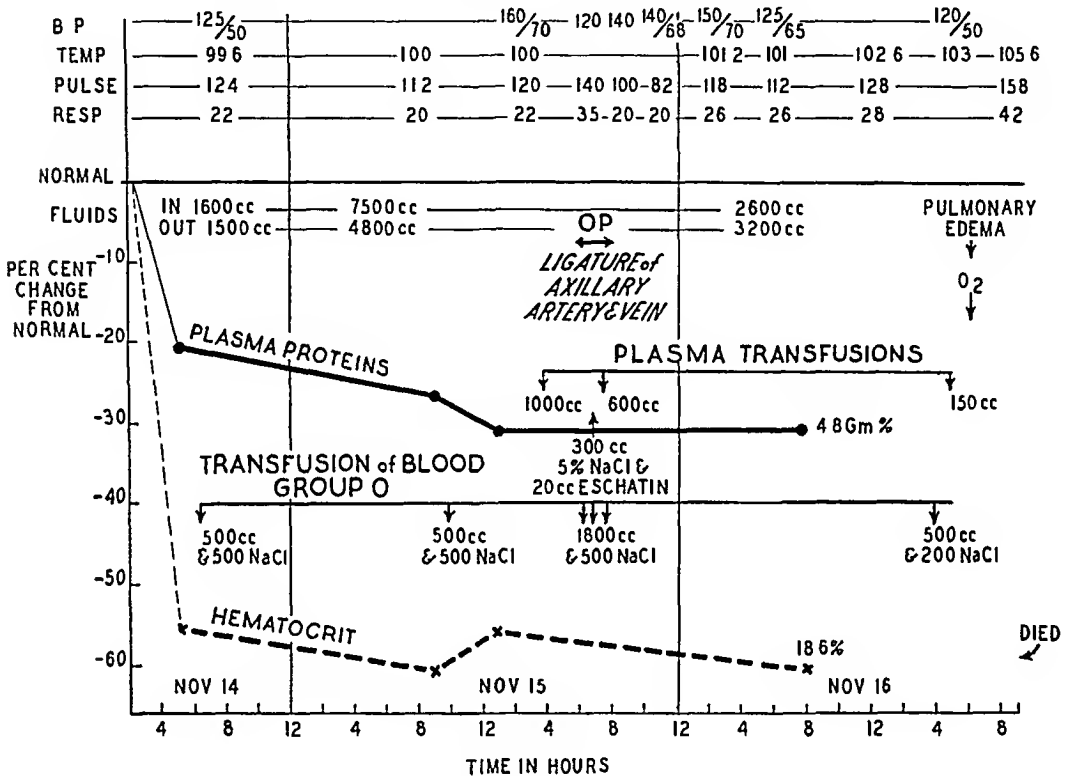


CHART I

Procedure "After making an incision through the pectoralis major muscle, more or less parallel to the clavicle, which itself was about 4 cm beneath the skin, the enormous hematoma or clot was found. This was evacuated in part and instantly a forceful gush of bright blood appeared from the region of the axillary artery. The bleeding was controlled by finger pressure against the clavicle above the site of laceration, after which, with suction and sponging, the lower end of the proximal axillary artery could be identified and clamped, controlling the hemorrhage." Artery ligated and wound closed about drain.

N.B. "Before beginning the operation the systolic pressure was 100, at the termination the systolic pressure was 140, color improved. Two transfusions were started in the left arm and right ankle before the surgical procedure was begun. These were allowed to run slowly until the pectoralis major had been cut through and the clot evacuated, and during this period of critical bleeding both transfusions ran at full rate." In addition to 1,800 cc of blood, he received 600 cc of recalcified plasma, 300 cc of 5 per cent NaCl, and 500 dog units of adrenal cortical extract. After operation

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500 cc of saline with 5 Gm of Na sulfadiazine. At 11 30 P M the patient's condition was remarkably improved, color much better. Blood pressure 140/68, pulse 82.

Third hospital day. Patient's temperature started to rise, and he complained of increasing pain in his arm and hand, requiring sedation. There was some oozing on the dressing, but this was not excessive. His condition, though critical, was not alarming. On account of the persistingly low hematocrit (18.6 per cent) and plasma proteins (4.8 Gm per cent), a transfusion of citrated blood was given at 3 15 P M. This was followed by plasma. Because of signs of pulmonary edema, the plasma was stopped after 150 cc. The temperature before the blood transfusion was 103° F and, after 105.6° F. Patient died at 9 10 P M, 26 hours after operation. The blood was rechecked and found compatible. Plasma from the same pool had been administered to two other patients without reaction.

Postmortem Examination—Gross. The pertinent descriptive data are limited to the thorax and upper extremities. The mouth and nasal passages were filled with white frothy fluid and the mucous membranes were quite pale but slightly cyanotic. The neck was of normal contour except for soft swelling and bluish-purple discoloration of the subcutaneous tissues in the right supraclavicular fossa. This also extended over the entire right shoulder, the right anterior chest wall, right axilla, and the medial surface of the right upper arm. From a point in the midsternal line, 3 cm below the sternal notch, extending laterally to the superior surface of the right shoulder was a recent surgical incision 28 cm long. A cigarette drain protruded from the center of the incision, and thin sanguineous fluid exuded from the wick and about the drain. The upper extremities were of normal contour and color, except for edema of the left forearm, resulting from recent infusion which had extravasated. When the muscles were dissected from the chest wall, a large amount of dark red clotted blood, as well as fresh unclotted blood, was found in the right axilla, and between the right pectoralis major and minor. The muscles themselves were two to three times their usual thickness because of the extravasation of blood into their sheaths and between their fibers. There was no fracture of the clavicles, ribs, or sternum.

The right axillary artery in its first portion was intact, its lumen patent and 4 Mm in diameter. No gross change was noted in its wall. The distal part of the second portion of the artery, posterior to the clavicle, had been ligated with a heavy braided silk suture and its lumen obliterated proximally over a distance of 7 Mm by a firm blood clot. For a distance of 1 cm above the ligature, there was a fusiform dilation of the vessel with its lumen measuring 6 Mm across and its wall thinned-out to approximately 0.5 Mm in contrast to the 1 to 1.2 Mm thickness in the first portion of the artery. A thin, white line of tissue, about 0.5 to 1 Mm thick, bridged the lumen, separating the clot into two portions. The third portion of the artery could not be found. The brachial artery was located in its sheath with vein and nerves, in the right axilla 3 cm below the ligated stump of the axillary artery. It had not been ligated and its lumen was slightly dilated by a firm, friable, adherent blood clot for a distance of 2 cm. A white line of tissue, like that seen in the axillary artery, bisected the clot. Below this clot, the lumen was patent and the vessel wall normal in appearance.

The right axillary vein had been ligated and sectioned at a point level with that of the artery. Its lumen, distal to the ligature, contained a soft blood clot. Its wall was intact and apparently normal. The left axilla, with its veins, arteries, and nerves showed no evident deviation from the normal.

Thoracic cavity. The right pleural cavity contained approximately 500 cc of thin, bloody fluid. No adhesions were present and the lung was expanded. The intact parietal pleura was smooth, but outside of it was dark purplish extravasated blood extending over the entire upper portion to the level of the sixth rib anteriorly and posteriorly. The left pleural cavity also contained 500 cc of thin bloody fluid. The left lung was expanded and both layers of pleura were intact. The hemorrhage had extended into the soft loose

tissues of the mediastinum and up into the base of the neck. Sixty cubic centimeters of pericardial fluid was blood-tinged, but the lining of the sac was intact, white and glistening. The aorta was grossly normal except for hemorrhage in its adventitia in its upper half. The right lung weighed 640 Gm, the left 800 Gm. Edema was the only positive finding.

The remaining viscera were not unusual.

*Microscopic**—Right axillary artery. The lumen of the vessel just above the ligature was occluded by a fresh thrombus, and a recent small dissecting aneurysm was found. It began at a point approximately 5 Mm above the ligation in a shallow rent in the



FIG 1—Proximal Right Axillary Artery (trichrome stain). Fibrosis and dissection of arterial wall (Low power)

intima and extended distally into the media throughout the dilated distal part of the artery (Fig 1). The same change was seen in a section taken through the proximal portion of the brachial artery, into which the dissecting aneurysm had apparently extended. In several sections, just proximal to the ligature, the hemorrhage penetrated the adventitia and the surrounding fibro-areolar tissue.

The changes in the wall of both axillary arteries, the celiac axis, and the renal arteries were most unusual and worthy of detailed description.

Localized segments of the wall of the *right axillary artery* were thickened. In these locations the internal elastic lamella could not be identified and the intima and media appeared as one thick mass of pale musculo-connective tissue containing widely separated spindle cells embedded in a matrix of loose unstained fibrils. *Elastic tissue stain* revealed

*All sections of the arteries were stained with hematoxylin and eosin, Masson's trichrome, elastic tissue (Hart's modification), Levaditi, and Gram.

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numerous delicate, fragmented, sometimes granular elastic fibers in these thickened areas, and only in a few portions of the vessel wall was the regular alignment of medial elastic lamellae encountered, and this usually in the thinner portions of the vessel wall (Plate IA) *Trichrome stain* proved the abundance of irregular, delicate collagen fibers between the elastic tissue as well as a paucity and focal absence of muscle cells. The deepest layers of media and adventitia were merged throughout two-thirds of the circumference of the vessel and by trichrome stain were found to be composed of dense, blue-staining, acellular fibrous tissue (Plate IB). Well preserved erythrocytes and fragments of fibrin were present in the surrounding loose fibro-vascular tissues. Levaditi and Gram stain revealed no micro-organisms. The dissecting aneurysm, previously described, began in one of these thickened regions of the right axillary artery.

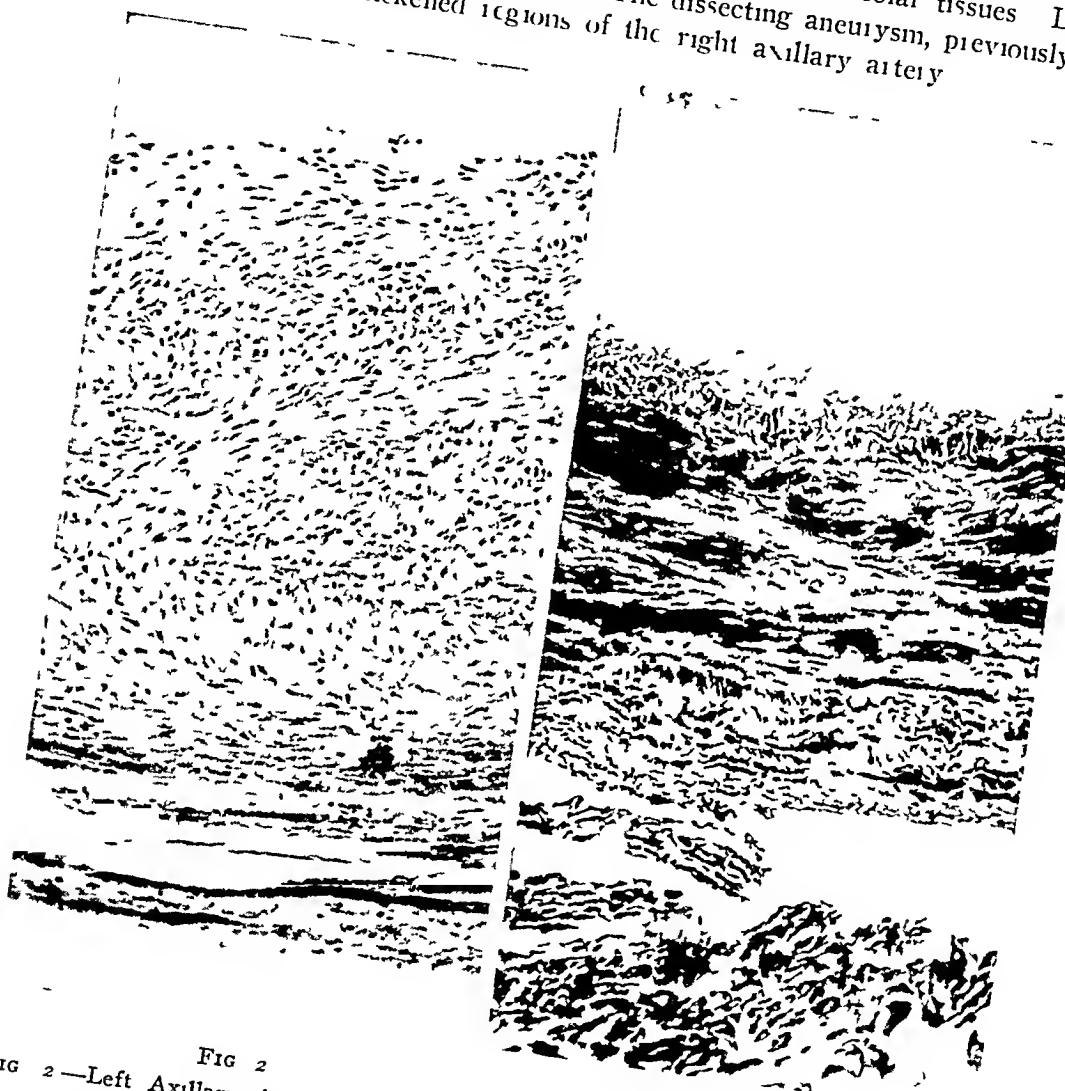


FIG 2

FIG 2—Left Axillary Artery (H and E stain) Disorderly arrangement of fibers (X110)

FIG 3

FIG 3—Celiac Artery (trichrome stain) Musculature in many places is defective and somewhat irregular in arrangement (X110)

In the *left axillary artery*, the irregular thickening of the wall, though present, was less pronounced. Intima and media could not be differentiated and the internal elastic lamella could not be identified (Fig 2). At several points the deepest layer of media and adjacent adventitia were fibrosed but not appreciably thickened. In many portions of the media, the normal arrangement of the elements was destroyed, and instead there was found a disorderly mixture of muscle cells, collagen, and elastic fibers with no circumferential alignment (Plate IC). By *elastic tissue stain* the intimal elastic lamella was rarely recognizable, the intima, in consequence, was not sharply differentiated from the media. In the inner layer of media there was condensation of elastic fibers, two or three

deep These were thin, quite delicate, and similar to those in the remainder and deeper portions of the media The deepest layer of media and adventitia were fibrosed and their line of demarcation indistinguishable

Other arteries The changes in the celiac axis, pancreaticoduodenal, and renal arteries, though much less intense than in the axillary vessels, were of the same general character (Fig 3) The musculature in many places was defective and somewhat irregular in its arrangement Often the bundles of muscle fibers were quite widely separated by loose fibrillar collagen and by elastic fibrils, fragmented and delicate, or condensed and granular

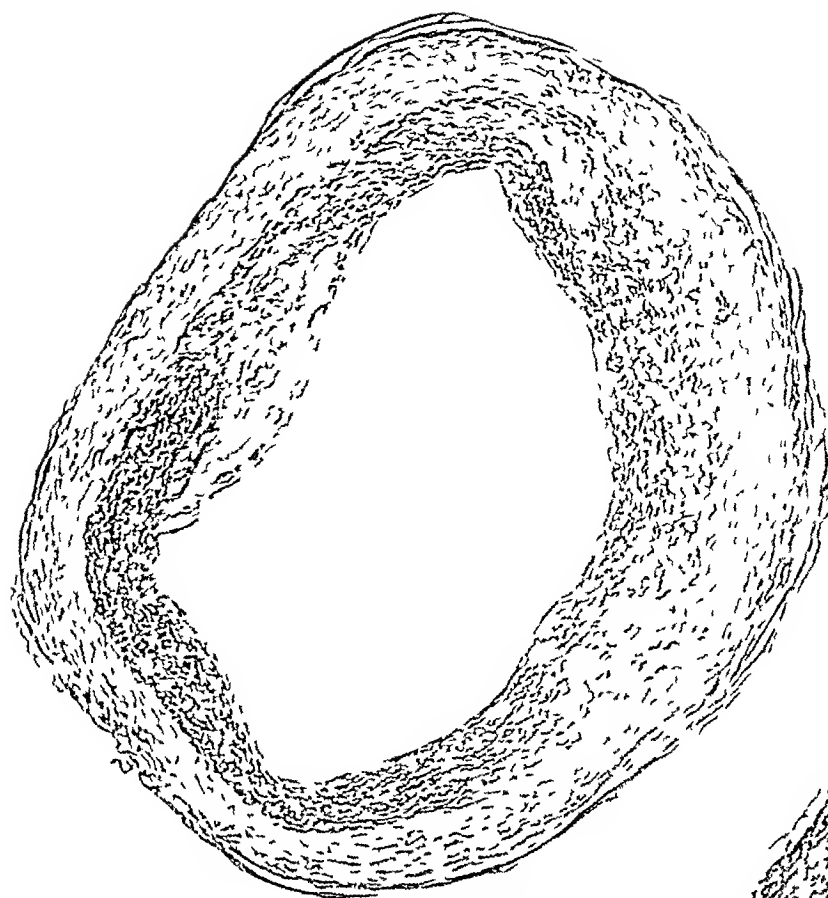
DISCUSSION—The question of support and the nature of therapy needs comment in this boy, who had been critically ill for four days, with an increasing mass in his right axilla accompanied by a rapidly falling red blood count and signs of circulatory insufficiency, as reflected by his pallor and episodes of syncope His admission hematocrit was 21.4 per cent and plasma proteins 5.54 Gm per cent He obviously needed blood, and, after determining his Rh factor, he was given fresh citrated blood on admission and just prior to operation To combat the hypoproteinemia he received 1,000 cc of recalcified plasma (plasma from which most of the fibrinogen has been removed by shaking with calcium chloride) This plasma assays between 70–90 mg per cent of calcium, 5–6 Gm per cent of proteins

During the operation, 1,800 cc of blood was transfused within a period of two hours This was *citrated* blood The total amount of citrate administered in 48 hours was 24 Gm In retrospect, this may have been *too* much, as he developed pulmonary edema and showed blood-tinged fluid in the pleural and pericardial cavities The dangers of too much citrate have recently been stressed^{1, 4} The decrease in ionized calcium in hypoproteinemia, graphically illustrated by Hastings and McLean,⁷ is of peculiar interest in this boy whose proteins continued to decrease

He should have been given *direct whole blood transfusions* on admission, and should have been operated upon then On account of his low proteins, he should have received *serum* rather than plasma Today, serum is being prepared at the Presbyterian Hospital Blood Bank for surgical cases with low proteins and for the treatment of infants with hypoproteinemia

The main interest in this case concerns the pathogenesis of the arterial lesions Three possibilities come to mind (1) The arterial lesions represent a constitutional malformation, (2) they are the effect of some unknown dietary deficiency, and (3) they are the late result of some vascular toxin upon the media A specific infectious etiology seems highly improbable in the absence of any inflammatory reaction, either local or systemic

It is difficult to produce any arguments either for or against the idea that these vascular changes are congenital or constitutional The history states that the boy had always been frail and had bruised easily, this might be taken as indicating vascular fragility The literature on congenital hypoplasia of blood vessels refers chiefly to the aorta and the cerebral arteries The somatic vessels seem to have been little investigated from this point of view The changes described by Hansemann, Askanazy, Orlansky, and Wiesner³ do not tally with those found in this case, nor is there any record of such

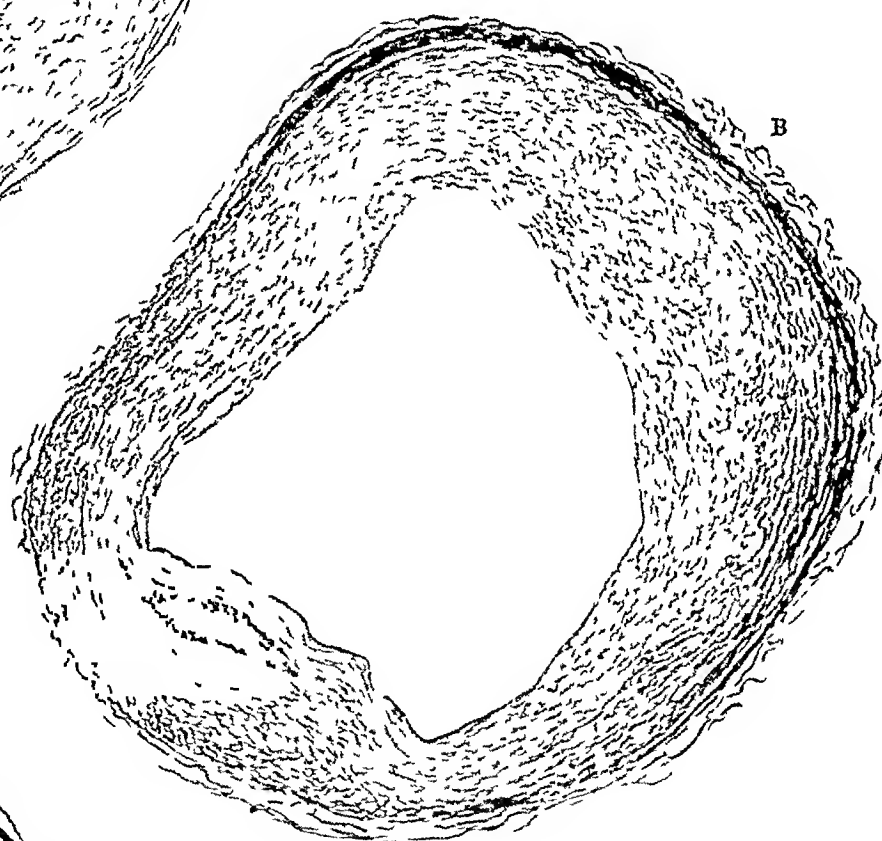


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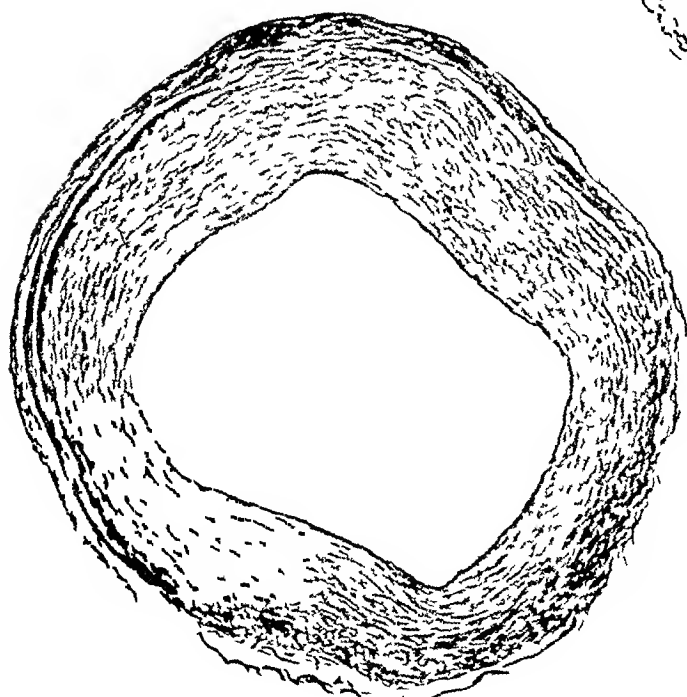


A—Right Axillary Artery (elastic tissue stain) This reveals numerous delicate, fragmented, sometimes granular elastic fibers in these thickened areas, and only in a few portions of the vessel wall is the regular alignment of medial elastic lamellae encountered, and thus usually in the thinner portions of the vessel wall

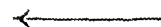
B—Proximal Right Axillary Artery (trichrome stain) An abundance of irregular, delicate collagen fibers between the elastic tissue as well as a paucity and focal absence of muscle cells. The deepest layers of media and adventitia are merged throughout two thirds of the circumference of the vessel, and by trichrome stain are found to be composed of dense, blue staining, acellular fibrous tissue



B



C



C—Left Axillary Artery (elastic tissue stain) The intimal elastic lamella is rarely recognizable. The intima in consequence is not sharply differentiated from the media. In the inner layer of the media there is a condensation of elastic fibers, two or three deep. These are thin, quite delicate, and similar to those in the remainder and deeper portions of the media. The deepest layer of the media and adventitia are fibrosed and their line of demarcation indistinguishable

congenital hypoplasia leading to spontaneous rupture except in the military cerebral aneurysms. On the other hand, the local defects in the vascular smooth muscle, with derangement of the normal relation between muscle fibers, elastic fibers, and connective tissue, suggests an architectural anomaly rather than cicatrization from previous destruction.

Vitamin deficiency has also been considered. This child lived in a period of deprivation during the last four years of life in France, and presumably had suffered the dietary restrictions incident to the war. However, we have no information regarding specific vitamin deficiencies in his diet, nor have similar vascular lesions been recognized to result from deficiency of any of the known vitamins. Actual necrosis of muscle fibers, with calcification, as described by Oppel⁸ in vitamin A deficient rats, was not present in this case.

At the age of one year, the child was immunized against diphtheria. Eleven years later he had diphtheria. It is not definitely known whether he received antitoxin at this time. Subsequently, at the age of fourteen, he received, however, two injections of combined diphtheria and tetanus toxoid, two months apart. In view of this history, the question may be raised as to whether the vascular lesions may be attributed to the diphtheria toxin. It is well known that medial degeneration of the aorta, usually with calcification, may be readily produced in rabbits by diphtheria toxin.² However, in this case there is no necrosis or calcification, or destruction of elastic fibers. The lesions were confined to the larger peripheral vessels and were not present in the aorta. These points speak against their having been caused by diphtheria toxin.

We have found few references of similar cases, but one most similar is reported, in 1928, by Koch⁵. A 22-year-old athlete engaged in a variety of training exercises, after a test in swimming (breast-stroke), experienced pain in right shoulder. Shortly thereafter, he lifted a 50-Kg weight on a machine, this was followed by a very acute pain in the right arm, thorax, and shoulder, with faintness, vomiting, dyspnea. After six days, he felt somewhat better and started for the moving picture theater, but collapsed on the street. He partially recovered, but died suddenly in bed eight days later, 15 days after attack. *Autopsy*. Old and recent hemorrhage into pleural cavity. Complete tear across right subclavian artery, 3 cm distal from origin from innominate. The site of rupture was surrounded by aneurysm-like sac formed by adventitia. The right leaf of diaphragm showed a 15-cm tear involving muscle and overlying pleura. Microscopic examination disclosed no changes in arterial walls to explain the spontaneous rupture, but details are not given. Heart and other vessels were described as normal. Another somewhat similar case is reported by Longland,⁶ in which "all vessels were normal and the ruptured vessel showed one departure from normal in that some of the muscle nuclei in the neighborhood of the rupture were pyknotic."

In reviewing cases of spontaneous rupture of the inferior epigastric and internal mammary arteries, we found that practically all of these vessels

were the site of known and familiar changes, *ie*, periarteritis nodosa, Monckeberg's sclerosis, arteriosclerosis, aneurysm resulting from arteriosclerotic changes, medial necrosis, or some type of arteritis. In the last case, there was usually a history of some relatively recent infectious disease.

SUMMARY

A case of spontaneous rupture of the right axillary artery following slight exertion, in a 15-year-old boy, is described.

Study of the large peripheral arteries showed an histologic malformation in the arrangement of the various components of the arterial wall. The pathogenesis of these lesions is briefly discussed, but no conclusion reached as to etiology. The descriptive term, "arterial myopathy," is suggested to designate these unusual changes which appear to have resulted either from primary developmental defect or secondary loss of medial musculature.

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AN UNUSUAL CASE OF MECKEL'S DIVERTICULUM

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AND

LT. COL. MEREDITH G BEAVER, M C., A U S

MECKEL'S DIVERTICULA have been grouped, roughly, into four clinical types (1) Catarrhal inflammation, with or without associated regional complications, (2) those producing intestinal obstruction, (3) gangrene of Meckel's diverticulum, and (4) peptic ulcers due to the presence of ectopic gastric tissue¹ Although it is not uncommon to discover a persistent Meckel's diverticulum falling into one, or even perhaps two, of the above groups, it is rather rare and unusual, we feel, to encounter one which embraces three of these types

The case we are reporting presented a galaxy of abnormal findings Not only was the diverticulum abnormally long, but it had also undergone acute inflammatory changes, it had produced an almost complete small bowel obstruction, it had ectopic gastric mucosa, which had undergone peptic ulceration, and, to make the case complete, was associated with a pathologic diagnosis of early acute appendicitis This combination of pathology, namely, acute Meckel's diverticulitis, intestinal obstruction, peptic ulceration, and acute appendicitis, is of sufficient rarity and interest to warrant being reported

Case Report—The patient, age 20, was admitted to Torney General Hospital, April 10, 1944, stating that he had been ill some 36 hours prior to admission His illness consisted of lower abdominal cramps, without diarrhea Five hours prior to admission these cramps, which had occurred at intervals of five to ten minutes and had been moderately severe, had been replaced by a persistent severe subumbilical and right lower quadrant pain There had been no melena or dark stools The patient had vomited only once He had had no bowel movement for two days prior to admission, nor had he had any previous similar attacks There were no symptoms referable to his cardiorespiratory, genito-urinary or eye, ear, nose and throat systems

His family history was noncontributory His previous personal history revealed that he had had the usual childhood diseases History which was obtained subsequent to operation revealed that until the age of six he had had recurrent drainage and bulging of the umbilicus This had been quite severe and had necessitated frequent visits to the doctor The umbilicus was finally cauterized, and the drainage stopped at the age of six

Physical Examination—The patient was a well-developed and well-nourished male, who appeared to be semi-acutely ill There was moderate cyanosis of the lips and skin Temperature, 100° F, pulse, 120, respirations, 18

Essential physical findings were limited to the heart and abdomen The heart was of normal size There was an aortic systolic murmur which was transmitted to the vessels of the neck The cardiologist felt that this murmur was functional in character The electrocardiogram was reported as being normal The abdomen was of normal contour There was voluntary and involuntary guarding and tenderness, both subumbilically and in the right rectus muscle, just to the right and at the same level of the umbilicus The tenderness in this area was rebound in character and

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pressure on other points of the abdomen referred the tenderness to the right lower quadrant. There were no masses or viscera palpable. Rectal examination revealed exquisite tenderness high in the right rectal vault.

Laboratory studies revealed a white blood count of 12,400, with 83 per cent neutrophils. Urine was negative. *Preoperative Diagnosis* Acute appendicitis.

Operation—Under nitrous oxide and ether anesthesia, a McBurney incision was

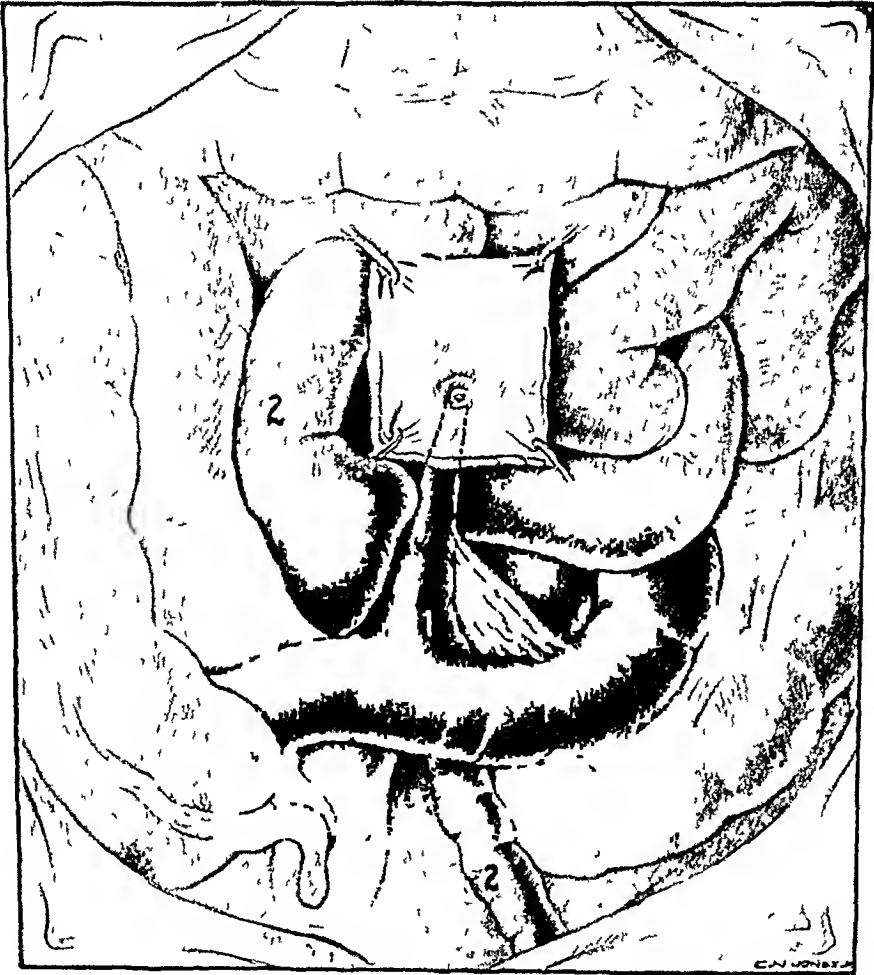




FIG. 1

- 1  TERMINAL ILEUM AND MECKEL'S DIVERTICULUM ARISING FROM IT AND ATTACHED TO THE UMBILICUS
- 2  DILATED AND COLLAPSED PORTIONS OF THE OBSTRUCTED SMALL INTESTINE

Photograph of the drawing through the courtesy of the U S Army Signal Corps

made. The appendix appeared to be grossly normal and was removed. Exploration of the abdomen revealed a diverticulum arising about ten inches proximal to the ileocecal valve. This diverticulum had its own mesentery and measured approximately 4.5 inches in length. At its tip it was attached to the under surface of the umbilicus. At this point of attachment the diverticulum was edematous and indurated, and was surrounded by a greatly thickened omentum. There was a rather marked increase in turbid peri-

toneal fluid At the tip of the diverticulum there appeared to be a perforation around which the omentum had wrapped itself The Meckel's diverticulum, acting as a band, had permitted the terminal ileum to herniate beneath it so that there was almost a complete small bowel obstruction The ileum proximal to this band was rather markedly dilated, while the ileum lying in the pelvis was collapsed (Fig 1) There were no pathologic changes in the bowel wall To facilitate the operative procedure the rectus muscle was transected and the entire diverticulum, together with its attachment to the umbilicus, exposed The diverticulum was freed from its attachment to the umbilicus After transecting and ligating its mesentery, the diverticulum was excised over a Payr clamp The resection of the diverticulum released the obstruction, permitting the distended bowel to resume its normal caliber Sulfanilamide crystals were sprinkled freely into the wound, and the wound closed in layers without drainage

Pathologic Diagnoses The removed specimens consisted of (1) Meckel's diverticulum, gastric type (2) Foreign body in Meckel's diverticulum, with erosions of mucosa and formation of early gastric ulcer (3) Acute appendicitis, early (4) Hyperplasia of lymphoid tissue of appendix, advanced The pathologist noted that this was an interesting specimen of Meckel's diverticulum which was lined with gastric mucosa of both a fundal and pyloric character A foreign body, presumably a wood splinter, had become impacted causing erosion and partial digestion of the damaged mucosa, similar in type to that seen in gastric ulcers (Patient stated that he had had the habit for many years of chewing match sticks, and one of these may have been the foreign body observed by the pathologist)

An interesting incidental finding was noted by the pathologist This was a very early acute appendicitis, with a small focus of material in the exudate and diffuse catarrhal appendicitis, characterized by marked hyperplasia of the lymphatic apparatus

The patient made an uneventful postoperative course and was returned to duty

COMMENT—It is interesting to speculate as to which of this patient's pathologic conditions was responsible for his admission into the hospital It is thought that the intestinal obstruction was probably the primary pathology The history of recurrent, rhythmical pain, which the patient described as cramps, together with the findings at the time of operation of a small bowel obstruction, are evidence in support of this contention Certainly, the acute diverticulitis was an important contributory factor The fever, the leukocytosis, with the shift to the left of the polymorphonuclear element, are indicative of acute inflammatory changes which, together with the intestinal obstruction, probably cover the entire picture The intestinal obstruction was of the simple mechanical type and there was no evidence of strangulation to account for the leukocytosis and abdominal tenderness The finding of early acute appendicitis probably aggravated the complaint, but was not in itself responsible for the patient's picture

SUMMARY

An unusual case of Meckel's diverticulum has been presented. This case was most interesting in that it presented an acute Meckel's diverticulitis, associated with a peptic ulcer, intestinal obstruction, and, coincidentally, with an acute early appendicitis

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BRIEF COMMUNICATION

ABSORBABLE SPONGE TESTS*

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THE NONIRRITATING FOREIGN BODY which can be left in the tissues for one purpose or another has become a problem of more and more interest in all fields of surgery. Until very recently only nonabsorbable material was ever introduced in any considerable physical bulk, for instance steel plates and screws in open reductions of fractures. Absorbable solid material was limited to catgut which is slightly irritating, but, because it is absorbed, does not promote the persistence of infection. Nonabsorbable materials—silk, cotton and silver—are also slightly irritating, but are, obviously, introduced in very small quantity, and, if infection does not occur, induce a minimal foreign body reaction, finally becoming encapsulated by varying amounts of fibrous tissue. Large amounts of cotton in the form of gauze sponges or compresses when accidentally left in a wound usually lead sooner or later to trouble.

There are, however, situations in surgery, problems of hemostasis chiefly, and of prevention of adhesions, where it is highly desirable to be able to leave absorbable nonirritating material in considerable bulk in an operative wound or an accidental wound. Even before battle casualties gave renewed impetus to the search for absorbable sponge such investigation was in progress in many laboratories. As a result, a number of materials have already been tested and are now in the stage of clinical investigation. The most promising to date have been fibrin foam prepared from human blood, gelatin, and gauze or cotton rendered absorbable by oxidation.

Of necessity, these products must be constantly checked to insure against any alteration which might render them irritating or nonabsorbable. Minimal contamination may result in established infection if an irritating foreign substance *in bulk* is left in the wound. Moreover, new materials are proposed which likewise need to be checked in animal tissues. After a study of various tissue reactions to absorbable gauze and to other absorbable sponges in larger laboratory animals it became apparent that there was a need for a simple standard test of these materials in smaller, less expensive animals. Possible contamination had to be reduced to a minimum so that an irritating product could be evaluated without a second factor which might evoke a tissue response. *It is not possible to judge a solid foreign body in an open wound in a laboratory animal.* Moreover, it is extremely difficult to prepare the skin of most

* This work was carried on under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Columbia University.

Submitted for publication February 27, 1945

laboratory animals so that clean wound healing may be expected if a foreign body is introduced. If infection develops it may be suspected that the irritating properties of the material being tested have contributed to this result, but cultures should be sterile before a product is condemned. Extraordinary precautions, therefore, must be taken and in tests in somewhat over 100 white rats, an animal chosen after considerable trial and error, the following method has been found satisfactory, not too time-consuming and not too expensive. This is a method previously used by one of us (Lattes, University of Turin), for the study of transplantable animal tumors.

PROCEDURE

Nembutal anesthesia 4 per cent solution intraperitoneal, 1 cc for a 200-gram rat. It is better to have the anesthesia a little light and supplement with ether, open cone, if necessary. The animal is then tied on a rat board, and the whole back shaved with electric clippers and painted with 4.5 per cent iodine. Sterile instruments are used for each animal and discarded. The operator is masked, scrubbed and gloved, but does not change gloves unless he touches the skin of the animal by accident.

A transverse incision 2 cm long is made with scissors in the interscapular region. The scissors are then discarded and a tunnel is made by holding up the distal skin edge with forceps, introducing a clamp in the midline and pushing it toward the sacral region where it is opened to spread the very lax subcutaneous tissue a little. Every care is taken not to touch the skin edge. With the skin edge still held up so that the mouth of the wound is wide open a glass tube (7-Mm caliber) containing the sample to be tested is introduced, avoiding the skin edge, to the limit of the tunnel made by the clamp. A glass rod (4 Mm) is then run through the tube and the pledget extruded into the tissues. With the clamp and the forceps the two corners of the wound are held up by the operator, and the wound is closed with two Michel clips placed by the assistant. The final site of implantation is, therefore, 5 or 6 cm from the skin wound. Moreover, the animal cannot chew the wound in the interscapular region, as happened frequently when we formerly used the lower back for the incision.

Autopsy can then be performed on the day of choice. After chloroform the back is wet with 70 per cent alcohol so as to avoid contamination from flying hair. A U-shaped incision is made with the base of the U slightly cephalad to the skin incision, and the sides well out along the flanks. The whole flap of skin can then be pulled toward the tail, exposing the tunnel in the subcutaneous tissue and the site of implantation of the sponge. A culture can be taken from the tissues at this site if there is any inflammation. If the foreign body is still unabsorbed, in part or in whole, its relation to the tissues can be ascertained. It may lie wholly inert, or it may be encysted or encapsulated. These variations depend on the nature of the material under investigation. With irritating materials a cavity may be formed lined by fibrin and polymorphonuclear leukocytes, and containing

sterile purulent fluid With this technic it is gratifying to see how little tissue damage is done along the tunnel leading from the wound to the site of implantation There is a minimum of inflammation Where there has been interference with healing of the skin wound (ordinarily from trauma in the cage postoperatively) the site of implant is usually still protected by distance, and cultures will be sterile

The size of the trial pledget is a matter of choice It should be large enough to constitute a mass of appreciable physical bulk We have used a square centimeter of material The gauze has been 8-ply Cotton or other sponges are cut to approximately the same bulk Relative times of absorption of different materials, limited of course, to the reaction of this one tissue, can thus be roughly estimated Many factors, however, influence the rate of absorption, and any product released for clinical investigation should first be thoroughly studied in various tissues of larger animals

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